

***Windsor Air Quality Study***  
***L'étude sur la qualité de l'air de Windsor***

Windsor Air Quality Committee

Comité sur la qualité de l'air de Windsor

**Health Effects Assessment**  
**Appendices 1-24**

## **REPORTS OF THE WINDSOR AIR QUALITY STUDY**

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**WINDSOR AIR QUALITY STUDY:  
HEALTH EFFECTS ASSESSMENT  
APPENDICES 1 - 24**

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**WINDSOR AIR QUALITY STUDY:**

**HEALTH EFFECTS ASSESSMENT**

**APPENDICES 1 - 24**

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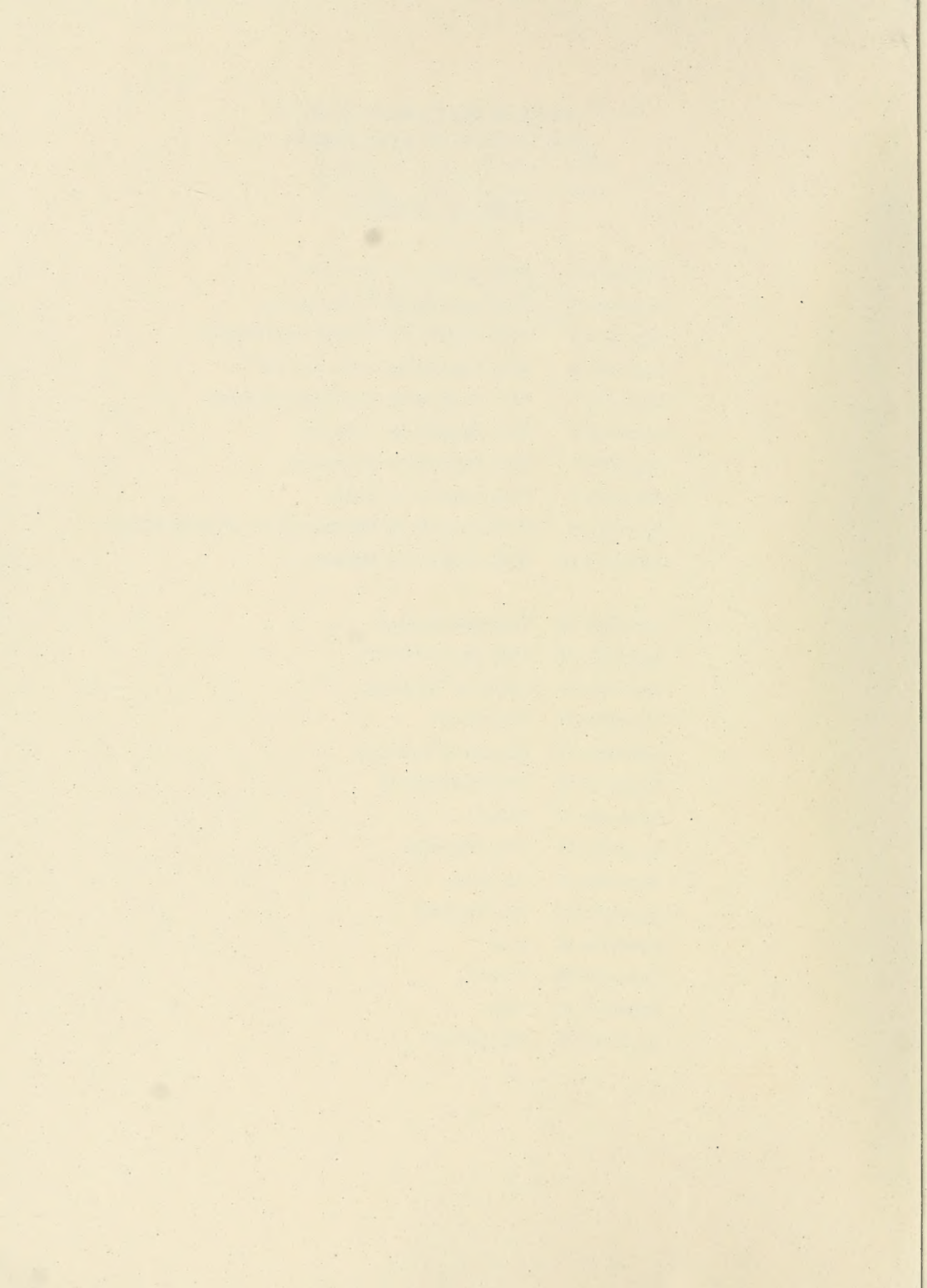
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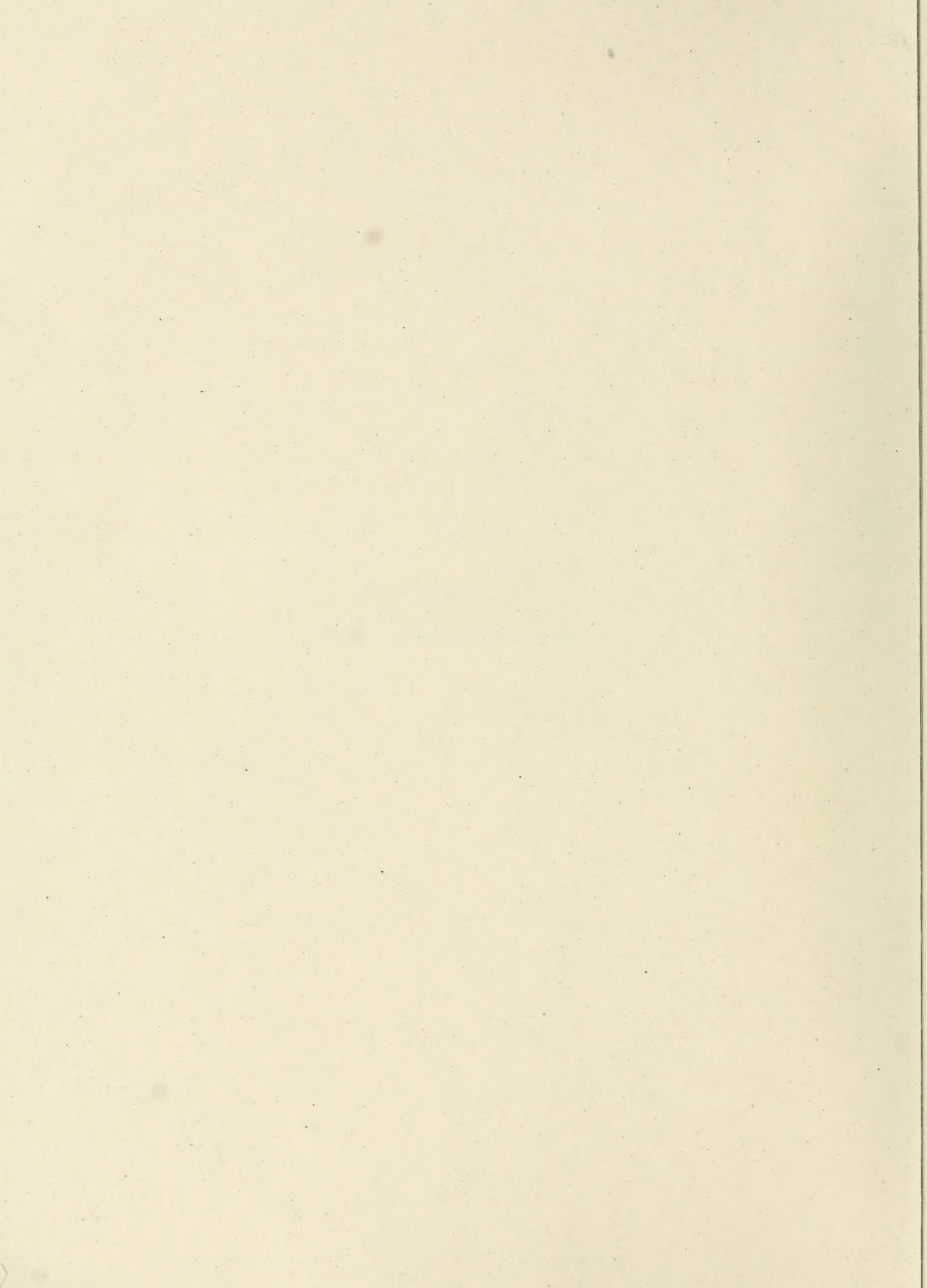
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## APPENDIX 1

### RISK ANALYSIS FOR BENZENE

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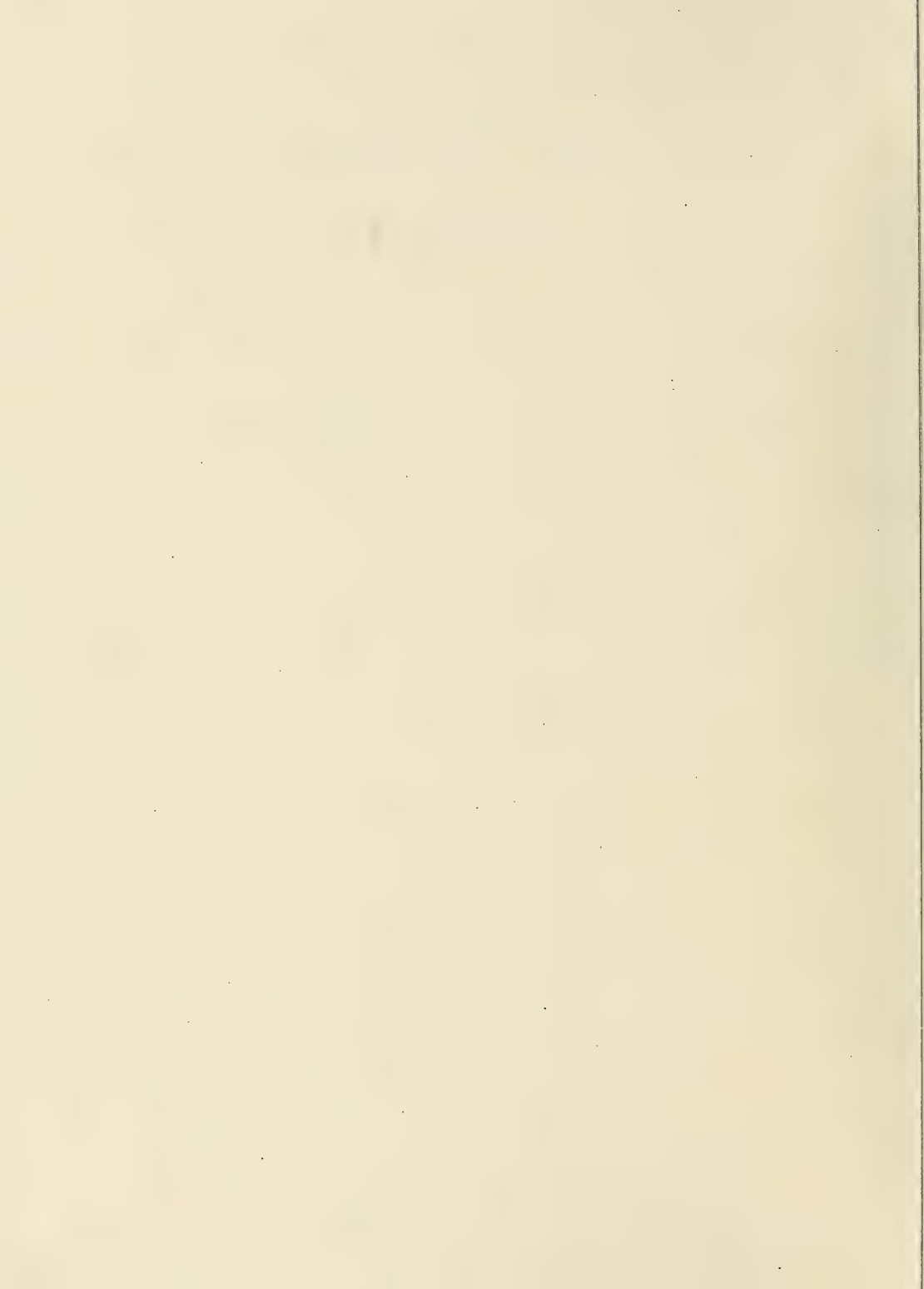
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## BENZENE

### DESCRIPTION and SOURCES of BENZENE

Benzene is a clear, colorless, volatile compound which has been commercially produced and used since the 1860's. It is a natural constituent of crude oil and is produced from forest fires and smoldering wood. It is also produced from cigarette smoke in homes and offices. Benzene is a constituent of gasoline and diesel fuel, generally comprising 1 to 3 percent of gasoline by weight. It is used as a raw material in the production of industrial chemicals which, in turn, are used to manufacture a wide range of products, including plastics, nylon, pharmaceuticals, and insecticides.

Benzene enters the environment during production, storage, transport, venting, and combustion of gasoline; during production, storage, and transport of benzene itself; during production of other chemicals from benzene; from coke oven and steel mill operations; and as a result of spills. In general, benzene has been detected in air, surface water, well water, raw and treated drinking water, industrial plant discharges, soil, food, and tobacco smoke.

Human populations are primarily exposed to benzene from the air, particularly in areas with heavy automobile traffic, around filling stations and airport operations, and near manufacturing plants which produce or use benzene.

#### 1. HAZARD IDENTIFICATION

##### 1.1 Absorption and Metabolism

Exposure of the general population to benzene occurs primarily *via* the pulmonary route<sup>14,21</sup>. However, a minimal amount may also be ingested through the food chain (*e.g.*, drinking water and garden produces) and, to a lesser extent, absorbed through skin contact<sup>9,14</sup>. Data regarding the inhalation absorption of benzene by humans consistently suggest a lung absorption factor of about 50% when exposure occurs at high doses for several hours<sup>9</sup>. It is likely that this fraction will be more important at the low levels of benzene generally found in the environment. Information gained from animal studies also indicates that humans would absorb benzene with relatively high efficiency in the gastrointestinal tract, while more limited penetration would occur through the skin<sup>9</sup>.

Following absorption into the blood through ingestion, inhalation, or dermal contact, benzene is widely distributed to tissues, with the relative uptake dependent on the perfusion rate of blood through tissues. Approximately 30% is present in blood; over half of the absorbed portion is translocated into adipose tissue, liver, and bone marrow, the principal target organ for benzene toxicity<sup>9</sup>. Metabolism occurs primarily in the liver and, to a lesser extent, in the bone marrow where benzene is converted to benzene oxide by enzymes of the cytochrome oxidase system. Benzene oxide, an unstable intermediate, further forms phenol. Other metabolites include catechol, hydroquinone, diol-epoxides, muconaldehyde, and conjugated phenolic compounds<sup>9,22</sup>. Benzene is excreted both unchanged *via* the lungs, and as the phenol, sulfates, and glucuronide-conjugated metabolites in the urine. Phenol, the major urinary metabolite of benzene, is frequently used for the biological monitoring of exposed individuals.

##### 1.2 Toxicology

The toxicological aspects of benzene have been reviewed in a number of reports<sup>6,9,22-25</sup>. The most sensitive target system for benzene toxicity appears to be the hematopoietic and the immune systems. The nervous system is also important in the context of acute toxicity, although it is of little relevance to the general population except in cases of poisoning, spills, and industrial accidents.

There is general agreement among the various investigators in the field of benzene toxicity that benzene metabolites, not benzene, are the primary toxic agents in the induction of hemato- and immunotoxicity. Indeed, several studies have demonstrated experimentally the capacity of benzene oxide, hydroquinone, phenol, catechol, and *trans, trans*-muconaldehyde to induce hematotoxic effects. It is possible that these effects find their etiology in the combined action of several benzene metabolites with hematopoietic precursor components. Benzene-induced hematotoxicity has been shown to involve alterations in the erythroid, myeloid, and lymphoid lineages, of which the lymphoid and myeloid lines appear to be the most sensitive in human. It should be noted, however, that the cellular events underlying these effects are still unknown. A reflection of this situation is that current areas of research on the mechanisms of benzene action involve, among others, the identification and characterization of the ultimate active metabolite(s), interaction studies among these metabolites, and the elucidation of the critical cellular receptor site(s) and mechanistic events that lead to toxicity.

In line with the involvement of the hematopoietic system as the primary target organ of benzene toxicity, it has been reported that humans exposed to this chemical have developed hypoplasia of the bone marrow with anemia, pancytopenia, and aplastic anemia<sup>26</sup>. In certain cases, myelodysplastic syndromes (MDSs) have also been observed. Interaction with the lymphoid lineage has been shown to result in decreased immunologic surveillance, a phenomenon responsible for the high incidence of infections experienced by chronically exposed individuals. In accordance with the occurrence of MDSs (a class of hematopoietic disorders that includes various preleukemia states), several individuals surviving the marrow depression have subsequently developed leukemia<sup>26,28</sup>, with the most frequently observed variant being acute myelogenous leukemia<sup>27</sup>. Certain of these hematotoxic effects have been reproduced in different species/sex/strain of experimental animals exposed by various routes<sup>23,29</sup>. However, an adequate model of leukemogenesis that reproduces the responses observed in humans has not been established yet. It has also been shown, both *in vitro* and *in vivo* and in experimental animals as well as in humans, that benzene induces aneuploidy and chromosomal aberrations<sup>8</sup>. On the other hand, it is not considered a mutagen<sup>9</sup>, although recent studies have provided some evidence of revertant activity in certain strains of *Salmonella typhimurium*<sup>36</sup>. It is believed that these genotoxic manifestations may be responsible for the carcinogenicity of benzene. Based on these considerations, benzene has been classified as a class A (human) carcinogen by the US EPA<sup>2</sup>, and a class 1 (human) carcinogen by the International Agency for Research on Cancer<sup>24</sup>.

Finally, there is little information on the developmental toxicity of benzene in humans, although it has been shown to be embryo/fetotoxic in animals<sup>9</sup>. Carcinogenicity is currently the most relevant end-point on which regulatory bodies base their risk assessment as neoplastic events are purported to occur at levels of exposure lower than those associated with other health effects (see Figure 1.1).

Generally, the effects as discussed, and more specifically the occurrence of cancer, have been detected following long term exposure to relatively high levels of benzene in a variety of situations, primarily occupational<sup>28,30-34</sup>. As a result, there exist presently a great deal of debate in the scientific community regarding the capacity of benzene to induce leukemia and associated effects in members of the general population exposed to levels 100 to 10,000 lower. Indeed, studies conducted in rodents and primates have demonstrated a significant degree of variability in the production of putative toxic metabolites as a function of intensity and rate of exposure<sup>35</sup>. Furthermore, these responses are highly dependent on the animal model (*i.e.*, mice *vs* rats *vs* primates), thus raising some doubt on their relevance as human surrogates. As a result of these uncertainties, the assessment and prevention of potential health effects for communities exposed to environmental levels of benzene are dynamic on-going processes that, most likely, will not be resolved with the present state of knowledge. A direct consequence of this situation is that the majority of air guidelines currently available are entrenched with several layers of conservative assumptions in order to provide a comfortable margin of safety. In other words, exposure to these levels would not be expected to result in significant mortality and/or morbidity in the general population. On the other hand, it should also be recognized that the unnecessary adoption of conservative assumptions

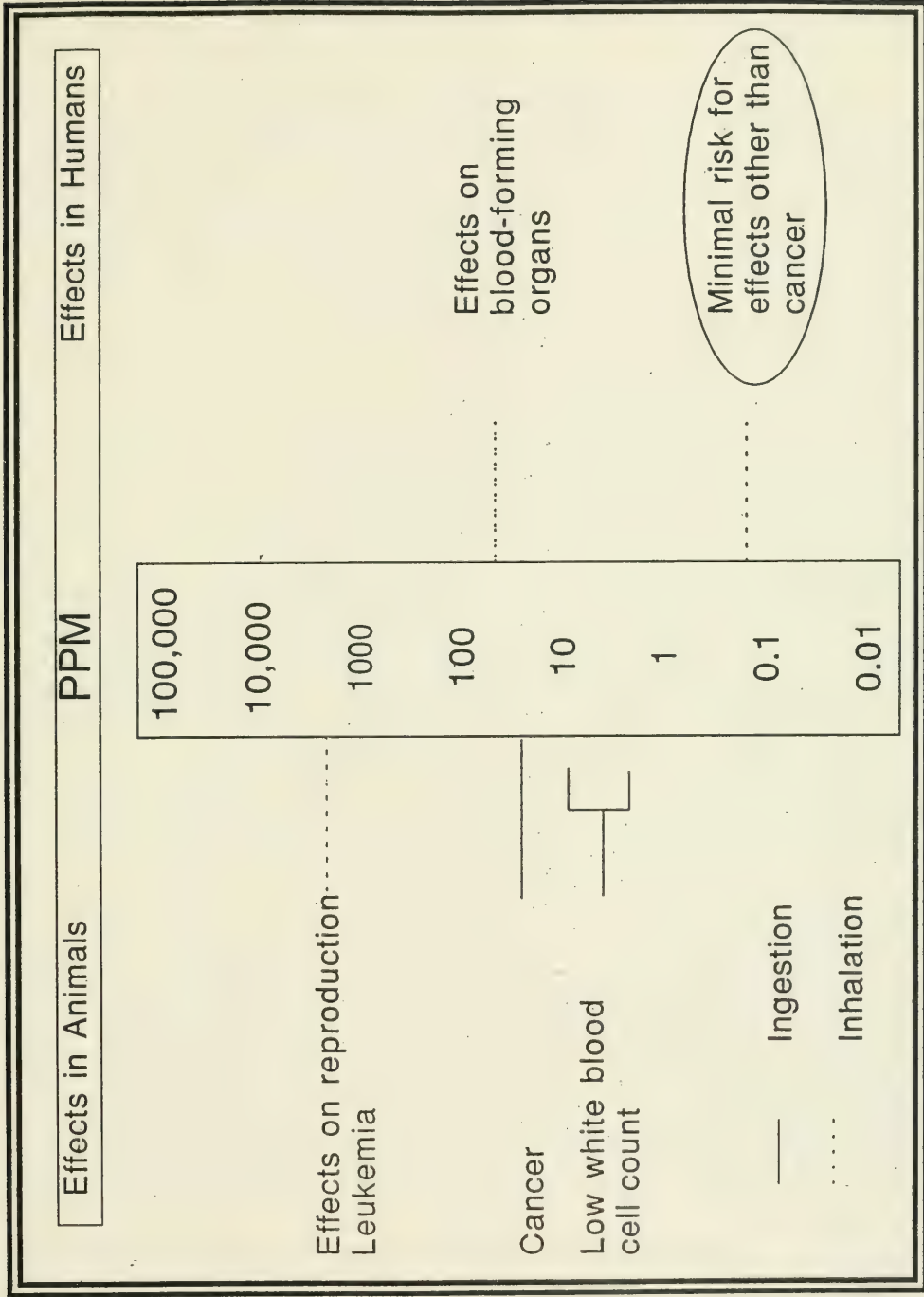


Figure 1.1 Summary of chronic effects associated with exposure to various levels of benzene (adapted from 9)(1ppm corresponds to 3.26 mg/m<sup>3</sup>)



imposes a significant burden to the concerned industries which could translate into adverse economic and social consequences.

## **2. DOSE-RESPONSE INFORMATION/CURRENT EXPOSURE GUIDELINES**

The uncertainties surrounding the potential toxicological effects of environmental benzene on communities have influenced significantly the methodologies used to set guidelines and permissible exposure levels. As previously noted, the adoption of reasonably conservative assumptions is warranted in this context in order to provide sufficient protection of public health. This section summarizes various health criteria values, that is, exposure guidelines and dose-response information that leading regulatory agencies (and other relevant sources) have proposed and consider appropriate for permitting, assessing, and characterizing risks associated with various exposures. Potential exposures to benzene are evaluated in section 3 and the risk characterization is presented in section 4.

### **2.1 Air Guidelines**

#### **2.1.1 Chronic, Non-Carcinogenic Health Effects**

The California Department of Health Services<sup>1</sup> has proposed for benzene, in January 1992, an inhalation chronic AEL (Acceptable Exposure Level) of 70  $\mu\text{g}/\text{m}^3$ . These values are used for the evaluation of the potential noncancer adverse health effects of long-term (chronic) exposures.

The US EPA's Integrated Risk Information System database<sup>2</sup> notes that the inhalation Reference Concentration (RfC) for benzene is under review. EPA defines an RfC as an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime.

In their treatise on air toxics and risk assessment, Calabrese and Kenyon<sup>38</sup> reviewed the toxicological evidence for benzene and suggested an Ambient Air Level Goal (AALG) of 160  $\mu\text{g}/\text{m}^3$  to prevent developmental effects.

Generally, the inhalation chronic AEL, AALG, and the inhalation RfC noted above are comparable in their use for assessing chronic effects (except carcinogenic effects) due to inhalation. It is expected that constraining environmental exposures of human populations to cancer-preventive levels of benzene should decrease to negligible levels, or simply eliminate depending on the end-point of concern, the probability of occurrence of chronic non-cancer health effects.

#### **2.1.2 Carcinogenic effects**

For the purpose of estimating cancer risk, the U.S. EPA<sup>2</sup> has established an inhalation unit risk of  $8.3 \times 10^{-6} (\mu\text{g}/\text{m}^3)^{-1}$  for continuous lifetime exposure to 1  $\mu\text{g}/\text{m}^3$  of benzene. This corresponds to a cancer potency factor of  $2.9 \times 10^{-2} (\text{mg}/\text{kg}\cdot\text{day})^{-1}$ . The U.S. EPA unit risk estimate is based on data extracted from three separate epidemiological studies. Equal weight was given to cumulative dose and weighted cumulative dose as well as to relative and absolute risk model forms. A conservative, linear one-hit model was used for extrapolation. The unit risk was the geometric mean of four point estimates using pooled and adjusted data from the different studies. Estimates based on other studies range over slightly more than one order of magnitude, with a geometric mean of  $2.7 \times 10^{-2} (\text{mg}/\text{kg}\cdot\text{day})^{-1}$ .

The California Department of Health Services (CDHS)<sup>1</sup> has established an inhalation unit risk of  $2.9 \times 10^{-5}$

$(\mu\text{g}/\text{m}^3)^{-1}$  associated with lifetime continuous exposure to  $1 \mu\text{g}/\text{m}^3$ . The corresponding (*i.e.*, calculated) inhalation cancer potency factor is  $1.0 \times 10^{-1} (\text{mg}/\text{kg}\cdot\text{day})^{-1}$ .

The World Health Organization (WHO)<sup>5</sup>, in its air quality guidelines publication, noted that at an air concentration of  $1 \mu\text{g}/\text{m}^3$ , the estimated lifetime risk of leukemia is  $4 \times 10^{-6}$ . This translates into a unit risk factor of  $4 \times 10^{-6} (\mu\text{g}/\text{m}^3)^{-1}$ , corresponding to a cancer potency slope of  $1.4 \times 10^{-2} (\text{mg}/\text{kg}\cdot\text{day})^{-1}$ .

Following a critical review of the available human database, the International Agency for Research on Cancer (IARC)<sup>39</sup> proposed in 1982 a unit risk factor of  $3.7 \times 10^{-6} (\mu\text{g}/\text{m}^3)^{-1}$ , as calculated by the WHO<sup>5</sup>. This corresponds to a cancer potency slope of  $1.3 \times 10^{-2} (\text{mg}/\text{kg}\cdot\text{day})^{-1}$ .

In Ontario, the ambient air quality criterion and the half-hour point of impingement standard have been withdrawn and new values are under development.

Finally, various jurisdictions have established annual air quality guideline values for benzene. For the jurisdictions of Indiana, Massachusetts, New York, Texas and the Netherlands the annual average guidelines range between  $0.12$  and  $120 \mu\text{g}/\text{m}^3$ <sup>3,4</sup>. It is noteworthy, in view of the large range of benzene concentrations allowed by these values, to recognize that some jurisdiction guidelines are based purely on risk assessment considerations, that is, on the evaluation of health effects in order to provide health protective values, and does not include consideration of technical, economic, and analytical feasibility or any of the other issues that are in the realm of risk management. Such is the case for the air guidelines proposed by the New York State Department of Environmental Conservation<sup>40</sup> and the Massachusetts Department of Environmental Protection<sup>37</sup>, both derived based on the US EPA's CAG unit risk factor. In some cases, risk management considerations were integrated in air guidelines, such as in the  $12 \mu\text{g}/\text{m}^3$  proposed in the Netherlands<sup>4</sup>. Indeed, although based on a risk assessment approach similar to that advocated by the WHO (*i.e.*, consideration of epidemiological studies with the application of the linear, non-threshold relative risk model), the final value proposed by the Health Council of Netherland integrates distinct risk management factors specific and relevant for that economy. It is clear, therefore, that any comparison of population benzene exposure to the Dutch air guideline will only provide a partial picture of the potential health risks. It should also be recognized that one risk management-based guideline may not be appropriate for other jurisdictions presenting with significant differences in social, economic, cultural, and political characteristics.

Occupational exposure guidelines have been developed for benzene. In the U.S., the Permissible Exposure Limit (PEL), established by the Occupational Safety and Health Administration (OSHA)<sup>6</sup> is  $1 \text{ ppm}$  ( $3260 \mu\text{g}/\text{m}^3$ ). The American Conference of Industrial Hygienists (ACGIH)<sup>6</sup> presently has a Threshold Limit Value-Time Weighted Average (TLV-TWA) of  $10 \text{ ppm}$  ( $32600 \mu\text{g}/\text{m}^3$ ) but in 1991 a revision to  $0.1 \text{ ppm}$  ( $326 \mu\text{g}/\text{m}^3$ ) was proposed and placed on the Notice of Intended Changes.

The current Ontario occupational guideline for benzene is  $16000 \mu\text{g}/\text{m}^3$  ( $4.9 \text{ ppm}$ ). A new value,  $1500 \mu\text{g}/\text{m}^3$  ( $0.5 \text{ ppm}$ ) was recently proposed<sup>7</sup> based on a recent review of five jurisdictions, with the most stringent value having been selected.

The above guidelines for atmospheric benzene are summarized in Table 1 below.

## 2.2 Other Route Guidelines

There appears to be no human studies regarding cancer effects after oral exposure to benzene. Rodents fed benzene have developed tumors in various glands and organs and also lymphomas, a variety of leukaemia. It is generally assumed, in the context of guideline development, that humans also will develop tumors if benzene is ingested<sup>9</sup>.

For the purpose of estimating cancer risk from oral exposures, the US EPA<sup>2</sup> has established an oral slope factor of  $2.9 \times 10^2$  (mg/kg-day)<sup>-1</sup>. The oral slope factor was derived based on the inhalation slope factor, since it is assumed that, once absorbed into the body, the effects of benzene do not depend on the route of exposure. In converting the slope factor to unit risk, the human respiratory rate was assumed by EPA to be 20 m<sup>3</sup>/day, inhalation and ingestion absorption were taken as 100%, an air concentration of benzene of 1 ppm was taken to equal 3.25 mg/m<sup>3</sup>, and an adult was assumed (ie. per EPA methodology) to ingest 2 L/day of water. The unit risk is estimated to be  $8.3 \times 10^7$  (ug/L)<sup>-1</sup>.

Studies with humans have shown that respiratory uptake (the amount of absorbed benzene following inhalation of the vapor) is about 50% whereas the amount retained (the amount of absorbed benzene that is not excreted via the lungs) was approximately 30%<sup>9</sup>. There are no human data on the gastrointestinal absorption of benzene, but studies with animals have shown that bioavailability by this route is generally at or above 90%. On the basis of this information, the conversion of the inhalation unit risk to the ingestion unit risk without allowing for differences in absorption may introduce a two-fold error.

The CDHS<sup>1</sup> potency of 0.1 (mg/kg-day)<sup>-1</sup> is 3.4 times that of the US EPA<sup>2</sup>. Part of this difference is explained by the CDHS choice of 0.1 which falls within the range of oral slope factors estimated by the CDHS and the US EPA (0.04 to 0.26). Furthermore, this value is the upper 95% confidence bounds on potencies derived from human data considered most credible by the US EPA (the US EPA estimate was the maximum likelihood estimate) and includes procedures used to correct for studies of short duration or with early mortality<sup>10,41</sup>.

The US EPA issued drinking water health advisories for the purpose of assessing short-term exposures only. These may not protect against cancer since they are generally higher than cancer-based guidelines and are intended primarily for emergency purposes. The ten-day health advisory is 235 ug/L for a 10 kg child drinking 1 L/day. Appropriate data for calculating a one-day health advisory are not available and a longer term advisory is not appropriate because of the potential carcinogenicity of benzene. The ten-day health advisory is based on a rat inhalation study. White blood cells were depressed at 103 mg/m<sup>3</sup> but not at 96 for up to 4 months. Assuming an absorption factor of 50%, the NOAEL for rats is 2.35 mg/kg-day. An uncertainty factor of 100 is used to allow for interspecies and intrahuman variability.

The current maximum allowable concentration (MAC) in drinking water in Ontario is 5 ug/L based on toxicological, feasibility, and analytical considerations as summarized in the Canadian water quality guidelines handbook<sup>42</sup>. The above ingestion guidelines are summarized in Table 1.

### 3. HUMAN EXPOSURE ASSESSMENT

#### 3.1 Inhalation

##### 3.1.1 Ambient Air Quality

Ambient levels of benzene have been measured at five fixed site stations in Windsor by two monitoring agencies, the Ontario Ministry of Environment and Energy and the Environmental Protection Service of Environment Canada. The measurements include four years of data and 254 samples, each collected over a 24 hour period. Concentration levels range from non-detectable to 11.65 ug/m<sup>3</sup>, with the median, mean (average), 90th percentile and 95th percentile levels being 2.59, 3.02, 5.57 and 7.36 ug/m<sup>3</sup>, respectively<sup>8</sup>.

TABLE 1. Summary of Exposure Guidelines for Benzene from Leading Agencies

GUIDELINE APPLICATION	AGENCY(IES)	ORIGINAL VALUE	CONCENTRATION ("Original Form" converted to these as applicable)			CALCULATED "ALLOWABLE" INTAKE (3)
			Unit Risk (1)	RsC (2) (1 x 10 <sup>-4</sup> )	RsC (2) (1 x 10 <sup>-4</sup> )	
INHALATION GUIDELINES						
Occupational	ACGIH, Ontario	326-32600 ug/m <sup>3</sup>	NA	NA	NA	6520 - 652000 (0.09 - 9.3)
Ambient Air Quality Guidelines	US states, Netherlands	0.12-120 ug/m <sup>3</sup>	NA	NA	NA	2.4 - 2400 (3.4 x 10 <sup>-5</sup> - 0.03)
Ontario Air Quality Guideline		Withdrawn;New values under review				
Chronic AELs/RfCs	CDHS	70 ug/m <sup>3</sup>	NA	NA	NA	1400 (0.02)
Inhalation Cancer Potency Factor	EPA CDHS WHO	See Unit Risk column	8.3 x 10 <sup>-4</sup> 2.9 x 10 <sup>-4</sup> 4.0 x 10 <sup>-4</sup>	1.2 0.34 2.5	0.12 0.034 0.25	for 1 x 10 <sup>-5</sup> risk: 6.8 - 50 (9.7 x 10 <sup>-5</sup> - 7.1 x 10 <sup>-4</sup> ) for 1 x 10 <sup>-4</sup> risk: 0.68 - 5 (9.7 x 10 <sup>-5</sup> - 7.1 x 10 <sup>-4</sup> )
INGESTION GUIDELINES						
Drinking Water Guideline	Ontario	5 ug/L	NA	NA	NA	7.5 (1.1 x 10 <sup>-4</sup> )
Oral Cancer Potency Factor	EPA	2.9 x 10 <sup>-2</sup> (mg/kg-day) <sup>1</sup>	8.3 x 10 <sup>-7</sup> (US EPA)	12	1.2	for 1 x 10 <sup>-5</sup> risk: 18 (3.4 x 10 <sup>-4</sup> ) for 1 x 10 <sup>-4</sup> risk: 1.8 (3.4 x 10 <sup>-5</sup> )

<sup>1</sup>For inhalation and ingestion guidelines, unit risks are expressed as ( $\mu\text{g}/\text{m}^3$ )<sup>1</sup> and ( $\mu\text{g}/\text{L}$ )<sup>1</sup>, respectively<sup>2</sup>For inhalation and ingestion guidelines, risk specific concentrations are expressed as  $\mu\text{g}/\text{m}^3$  and  $\mu\text{g}/\text{L}$ , respectively<sup>3</sup>Intake was computed by assuming, where applicable, an adult weight of 70 kg, a breathing rate of 20  $\text{m}^3/\text{day}$ , a water intake of 1.5 L/day. In all cases 100% bioavailability of the intake was assumed.



It is possible to estimate the daily intake of benzene associated with these measures of Windsor ambient air quality, recognizing that personal real exposures/intakes may be quite different as further discussed in section 3.1.2. Table 2 below shows these estimated intakes for two different receptors, i.e., an adult, and a child. It should be noted that these intakes were calculated based on 24 hour exposures and assume 100% bioavailability by the inhalation route.

**Table 2. Estimated Daily Intakes of Benzene Associated With Ambient Air Quality in Windsor**

Air Quality Measure (a)	Concentration ug/m <sup>3</sup>	Adult (b) ug/day (ug/kg-day)	Child (b) ug/day (ug/kg-day)
Median	2.59	52 (0.74)	13.0 (0.87)
Arithmetic Mean	3.02	60.4 (0.86)	15.1 (1.0)
90th percentile	5.57	111.4 (1.59)	27.9 (1.86)
a) Based on 254, 24 hour average samples b) Assuming the following weights and inhalation rates per day (ie. per 24 hour period): Adult: 70 kg; 20 m <sup>3</sup> /day Child: 15 kg; 5 m <sup>3</sup> /day			

### 3.1.2 Microenvironments

It is reasonable to assume that the daily benzene intakes associated with typical personal exposure patterns can be better estimated from various microenvironmental concentrations than from fixed site monitoring data. For the purpose of scoping population exposures, the set of typical receptors in Table 3 below was considered. Examples of the receptor types and/or their characteristics are also included in Table 3. Using benzene concentrations acquired in various microenvironments, either as part of the personal exposure or subsequent microenvironment study in Windsor, it is possible to scope out various typical personal inhalation exposure scenarios for the above receptors. The estimated daily intakes (in ug/day) of these receptors are summarized in Table 4.

A microenvironment, in which measurements were not taken, is the bathroom during bathing and showering.

Volatile organic chemicals will partition from the hot water during showering and bathing and be inhaled by the person in the bathroom. A simple one-compartment model has been developed that takes into account the air exchange between shower stall and bathroom and the rest of the house and calculates the maximum concentration -  $C_{a_{max}}$  - reached during showering<sup>11</sup>. The formula is

$$C_{a_{max}} = C_w f F_w T_d / V_a$$

Table 3. Receptors With Typical Personal Exposure Patterns

NAME OF RECEPTOR TYPE	CHARACTERISTICS	NAME OF RECEPTOR TYPE	CHARACTERISTICS
Average Office Worker (Non-smoking)	Eg. - Typical office worker (Based on Windsor volunteers and US EPA TEAM study; not smoking at home)	High Outdoor Receptor	Eg. - Construction workers; - Bicycle couriers - Police - Long distance runners
Average Office Worker (Non-smoker in a Smoker Environment)	Eg. - Typical office worker (Based on Windsor volunteers and US EPA TEAM study; smoking at home)	High Indoor Receptor	Eg. - 'Shut-ins' - Invalids - Elderly, non-mobile
Average Youth	Eg. Special exposures at shopping malls and athletic facilities (pools) in addition to school;	High Commuting Receptor	Eg. - Bus drivers - Taxi drivers - Delivery/Distribution Services
Average Child (Non-Smoker Home & No Exposure to Tobacco Smoke)	Eg. Similar to average office worker except 'School' replaces 'Office';	Active Receptor # 1	Eg. - 7 hr/week in Bingo Hall or Bar
Average Child (Non-Smoker Home & Typical Exposure to Tobacco Smoke)	Eg. Includes typical times that children may be in proximity to tobacco smoke, outside the home, based on activity pattern studies;		
Average Child (Smoker Home with Exposure to Tobacco Smoke)	Eg. Child living in a house where there is a smoker		

Table 4. Estimated Daily Intakes (ug/day) Associated with Typical Personal Exposures (See footnote 1.)

MICRO ENVIRONMENT	Air Concentration (ug/m <sup>3</sup> ) <sup>b</sup>	Average Office Worker	Average Office Worker	Youth	Average Child	Average Child	High Outdoor Receptor	High Indoor Receptor	High Commuting Receptor
		Non-smoker	Smoker Home Environments	Time spent (hrs)	Time spent (hrs)	Non smoker home/Typical exposure to tobacco smoke	Time spent (hrs)	Time spent (hrs)	Time spent (hrs)
Office	3.2/5.5 (m)	6.7(a)	6.7(a)				1.7		
School	3.2/5.5 (d)			6.7	6.7	6.7			
Home	2.8/5.8 (m)	13.3(b)		13.3	13.7	12.4	13.7	20.4	13.7
Commuting (in-transit)	15.7/40.7 (m)	1.0(a)	1.0(a)	1.0(f)	1.0(f)	1.0(f)	1(a)	1(a)	7.7
Urban (Outdoors)	3.0/ 5.6	2.6(a)	2.6(a)	2.6	2.6	2.6	7.6(g)	2.6	2.6
Home with smokers	3.6/7.0 (c)		13.7(b)			1.3(e)			
Shopping Mall/Market	6.8/13.9 (n)	0.4(i)		0.4(i)					
Bar or Bingo Hall	20.8/38.6 (k)								
INTEGRATED EXPOSURE (ug-hrs/m <sup>3</sup> )		84.9/ 174.8	94.3/ 188.0	84.9/ 174.8	83.3/ 171.6	84.3/ 173.1	82.3/ 172.1	80.6/ 173.6	167.1/ 407.4

TIME WEIGHTED AVERAGE EXPOSURE (ug/m <sup>3</sup> over 24 hr) (h)	3.5/7.3	3.9/7.8	3.5/7.3	3.5/7.1	3.5/7.2	3.4/7.2	3.4/7.2	7.0/17.0
INTAKE/DAY (UC/DAY) (h)	71/146	79/157	50/ 102	17/36	18/36	69/143	67/145	139/340



### Estimations:

- \* INTEGRATED EXPOSURE (ug-hrs/m<sup>3</sup>) = SUM OF [Microenvironment concentration x Time spent in Microenvironment]
- \* TIME WEIGHTED AVERAGE EXPOSURE (ug/m<sup>3</sup>) = INTEGRATED EXPOSURE/24 hr
- \* INTAKE/DAY (ug/day) = TIME WEIGHTED AVERAGE EXPOSURE x DAILY BREATHING RATE (ie. for Adult or Youth or Child as applicable)

### Footnotes:

- a.) TIME BUDGET ANALYSIS; Windsor '91 Summer PEP Study; Handout to Volunteers, May/92 (R. Bell)
- b.) Sum of 'Indoor, Home' and 'Indoor Other' in a.)
- c.) This value was obtained during the personal exposure study in Windsor from homes where smoking was permitted
- d.) Assumed to be same 'microenvironment' concentration that were measured by PEP study in the 'Office' environment.
- e.) Average time spent in proximity to tobacco smoke, in various locations outside the home, was approximately 1.3 hours, based on a study of children's activity patterns; (Ref: Study of Children's Activity Patterns, State of California, Air Resources Board, Contract No. A 733-149). Assume that benzene concentrations, when in proximity to tobacco smoke is represented by the median levels referenced in footnote "c," above.
- f.) Assume 1 hour is spent in the car per day.
- g.) For the 'high-outdoor' receptor, urban outdoor concentrations were assumed to be represented by the 'mean' and 90th percentile concentrations taken from the fixed site monitoring network. Also assume that for this group, the 6.7 hours of 'at work' exposure is divided so that 1.7 hours is spent in the office and 5 hours is added to the 2.6 hours of urban outdoor exposure for a total of 7.6 hours.
- h.) The first number is the 'mean'. The second number is the 90th percentile, if available; otherwise it is the maximum value measured.
- i.) Assumed that approximately 2.8 hours per week are spent in malls shopping; this was distributed over seven days yielding '0.4 hours/day' in malls.
- j.) Assumed that this receptor spends approximately 7 hours per week in a bingo hall or bar; this was distributed over seven days yielding '1 hr/day' in bingo halls or bars.
- k.) 'Bar' and 'bingo hall' data were combined to obtain these values, and these were assumed to be representative of both of these microenvironments.
- l.) Two additional typical personal exposure patterns that were evaluated but are not shown in detail in this table are the 'Average Child in a Smoker Home' and the 'Active Receptor # 1' as noted in Table 3 above. The corresponding intakes/day (ie. mean/90th percentile) for these two receptors are 20/39 and 84/170, respectively.
- m.) The 'mean' and '90th percentile' concentrations for the 'Office', 'Home' and 'Commuting' microenvironments were derived from the Summer 1991 and Winter 1992 personal exposure studies in Windsor.
- n.) These two values represent the minimum and maximum values in a limited data set.

where

$C_w$  is the water concentration (ug/L)

$f$  is the fractional volatilization rate with an assumed value of 0.75 (range 0.5 - 0.9)

$F_w$  is the volume of water used (L/h)

$T_d$  is the time spent in the shower or bath (h)

$V_s$  is the volume of the shower stall or bathroom (L)

The shower stall is assumed to have a volume of 2 m<sup>3</sup> or 2000 L and a showering time is 0.25 h. The average flow rate is 260 L/h and the maximum flow rate is 720 L/h<sup>11</sup>. The water concentration is 0.035 ug/L (s. drinking water section). The maximum concentration ( $C_{\text{max}}$ ) reached during showering is then 0.85 (for average flow) or 2.36 (for maximum flow) ug/m<sup>3</sup>.

The average calculated concentration is approximately half that of  $C_{\text{max}}$ , since  $C_a$  increases linearly with time and the exchange with the rest of the building is assumed to be minimal. The average inhalation rate is 20 m<sup>3</sup>/d for an adult or 833 L/h. The amount inhaled during the showering (0.25 h) is then 0.09 (for average flow) or 0.25 ug (for maximum flow).

An alternative scenario as described by the authors takes into account a full exchange between the shower stall and the bathroom, 15 minutes for a shower and an additional 15 minutes in the bathroom. The average concentration during the shower is  $C_{\text{max}}/2$  (since the concentration builds up gradually to  $C_{\text{max}}$ ), with  $V_s = 10$  m<sup>3</sup>, and during the remaining 15 minutes, the average concentration is approximately  $C_{\text{max}}$  (since dissipation of the maximum is slow). Under these circumstances,  $C_{\text{max}}$  is 0.17 or 0.47 ug/m<sup>3</sup> and the amounts inhaled are 0.05 and 0.15 ug.

Based on these two scenarios, the maximum inhalation intakes per day, are in the range of 0.05 to 0.15 ug/day. In view of the relatively small intake from this microenvironment as compared to other inhalation intakes, this can be considered negligible.

In order to place the above inhalation exposures (ie. intakes) in Windsor in perspective, it is appropriate to compare them to daily intakes of people who smoke.

### 3.1.3 Smoking.

Smoking is the largest anthropogenic source of background human exposure to benzene. Several estimates are available:

- a smoker of 32 cigarettes a day (the USA average) inhales about 1.8 mg/day or about 56 ug/cigarette. The median benzene concentrations in homes with smokers were about 50% higher than in homes with non-smokers<sup>9</sup>;

- Hattermer-Frey *et al*<sup>14</sup> quote three estimates: 30, 40 and 57 ug/cigarette. Nonsmokers who live with smokers have about 30-50% higher benzene levels in their breath than nonsmokers who did not live with a smoker.

- Holliday and Park<sup>13</sup> cite a 1983 paper by Higgins *et. al.*, who found values ranging from 94 ug/cigarette for a high-tar cigarette to a low of 0.07 for an ultra-low tar cigarette.

A person who smokes a pack a day (25 cigarettes) would therefore inhale an average of 1125 ug/day (45 ug/cigarette). The lower and upper bounds would be 1.8 and 2350 ug/day.

Non-smokers who are heavily exposed to environmental tobacco smoke inhale the equivalent of 1/3 to 3 cigarettes per day or, on an average (assuming 45 ug/cigarette), 15 to 135 ug of benzene/day (Blot and Fraumeni)<sup>19</sup>. Vainio<sup>43</sup> states that the exposure of non-smokers to environmental tobacco smoke would be about 1% of that of active smokers or 0.02 to 24 ug/day, whereas Remmer<sup>20</sup> gives as an upper limit the equivalent of only 1/5 of a cigarette per day or about 9 ug/day (assuming 45 ug/cigarette). Hiller<sup>44</sup>, quoting other authors, gives intakes ranging from a low of 0.001 cigarette equivalents (CE)/hr or 0.01 CE/day, assuming 12 hr exposure, to a high of 27 CE/day. The higher value is clearly anomalous as the range claimed by the other authors is 0.001 to 0.2 CE/hr. The lower value gives an intake of 24 ug/day (assuming 45 ug/cigarette).

It is also important to place the inhalation exposures (ie. intakes) in Windsor into perspective, relative to general exposures from other media (ie. see section 3.2).

### 3.2 Other Routes

In this section, possible non-inhalation routes of exposure (ie. ingestion and dermal) are estimated.

#### 3.2.1 Ingestion of Food

There are no analyses of benzene in food from the Windsor area. In general, there is little additional information. Holliday and Park<sup>13</sup> summarize the data available. The concentrations range from 0.2 ng/g in beans to a high of 1900 ng/g in hardboiled eggs. The median concentration is probably <50 ng/g and possibly <10 ng/g. They model a concentration in equilibrium with ambient air of 0.5-1.3 ng/g. The Agency for Toxic Substances and Disease Registry (ATSDR) Toxicological Profile for Benzene<sup>9</sup> reports concentrations in cooked meats of <10 to 20 ng/g and a high of 2100 ng/g in eggs.

Assuming a food intake of 1200-1500 g/day for children and adults and using the Holliday and Park equilibrium estimates (0.5 - 1.3 ng/g) leads to an ingestion of 0.6 to 2 ug benzene/d.

Hattemer-Frey *et al*<sup>14</sup>, using fugacity modelling, estimate that 0.02 ug/d of benzene are ingested, with 0.019 ug/d coming from produce. This is a factor of 30 to 100 less than the Holliday and Park<sup>13</sup> estimates.

These authors discuss the 1980 intake estimate by the National Research Council of the USA. The Council estimates that the average US urban exposure from all exposure routes is 850 ug/d, with the dietary component being as high as 250 ug/d. However, based on the mean USA adipose tissue concentration of 9.9 ug benzene/kg fat, the authors estimate that the long-term daily intake of benzene is 207 ug/d. The authors also suggest that the measured value may be inaccurate. On the basis of an equilibrium concentration of 3.45 ug/kg fat, calculated from a pharmacokinetic model, the long term daily intake is 72 ug/d. The NRC intake value appears therefore to be an overestimate.

#### 3.2.2 Drinking Water

The treated drinking water in Windsor was analyzed by the Laboratory Services Branch of the MOEE for benzene 15 times between 1990 and February, 1992 with a detection limit of 0.05 ug/L. Only two analyses were above the detection limit. If one assumes that the average concentration in those samples which are below the detection limit is 0.025 ug/L (ie. 1/2 the detection limit), then considered together with the two samples which were above the detection limit, the average concentration is 0.035 ug/L. This is above the reported background concentration of benzene measured in the USA of 0.006 ug/L (Ref. 14; Table 2).

The amount of benzene ingested is then based on the liquid ingestion volumes in the 1972 drinking water survey of Health and Welfare Canada<sup>15</sup>

- adult: median (1.49 L/d): 0.052 ug/d  
90th percentile (2.59 L/d): 0.091 ug/d
- child: median (0.76 L/d): 0.027 ug/d  
90th percentile (1.5 L/d): 0.053 ug/d

### 3.2.3 Soil

There are no analyses for benzene in the soils at Windsor. ATSDR<sup>9</sup> reports values from 2 to 191 ng/g near industrial sites. Hattermer-Frey *et al*<sup>14</sup> predict, based on fugacity modelling, that the soil concentration in equilibrium with ambient air is 0.06 ng/g. The amount of soil ingested by an adult is 20 mg/d and by a child 80 mg/d. Taking as the upper bound of concentration the value of 2 ng/g, the amount ingested by an adult is  $4 \times 10^{-5}$  ug/d and by a child,  $16 \times 10^{-5}$  ug/d.

### 3.2.4 Dermal

#### 3.2.4.1 During Showering and Bathing

EPA<sup>16</sup> has proposed a model for transient state dermal adsorption from water. The basic formula is, for  $t_{\text{sh}} < t^*$

$$DA_{\text{sh}} = 2K_p C_p (6t_{\text{sh}} / \pi)^{1/2}$$

where  $-DA_{\text{sh}}$  is dose absorbed per unit area per event ( $\text{mg}/\text{cm}^2 \cdot \text{event}$ );

$-K_p$  is the permeability coefficient ( $\text{cm}/\text{hr}$ );

$-C_p$  is the concentration in the water ( $\text{mg}/\text{cm}^3$ );

$-t_{\text{sh}}$  is the time spent showering or bathing ( $\text{hr}$ );

$-\tau$  is a number calculated from the skin thickness and diffusivity of the chemical in the skin ( $\text{hr}$ )

$-t^*$  is a number that is calculated from the value of B ( $\text{hr}$ ) ( $B = K_{ow}/10^4$ ;  $K_{ow}$  is the octanol/water partition coefficient)

Table 5-8 of reference 16 gives the appropriate values to use in the above equation ( $K_p = 0.11 \text{ cm}/\text{hr}$ ;  $\tau = 0.26 \text{ hr}$ ;  $t^* = 0.63$ ). It is assumed that a shower takes 0.25 hr/day and a bath 0.5 hr and that the water concentration is 0.035 ug/L (s. 3.2.2). The median skin surface area is 19400  $\text{cm}^2$  (reference 16, table 8-3) for an adult, the amount absorbed during a shower is 0.01 ug and during a bath, 0.014 ug. Similarly, the median skin surface area is 7310  $\text{cm}^2$  for a child (reference 16, table 8-4 for age 4<5 yr). The amounts absorbed are:

	<u>shower</u>	<u>bath</u>
adult	0.05	0.07 ug/d
child	0.02	0.03

#### 3.2.4.2 Contact With Soil and Dirt

Brainard and Beck<sup>17</sup> estimate that 10% of the benzene in soil that is in contact with skin will be absorbed



over a period of 12 hours. McKone<sup>12</sup> suggests that, on the basis of models, that if  $K_h$  (the dimensionless Henry's law constant) is  $> 0.1$ , the amount absorbed from soil is  $< 3\%$ .  $K_h$  for benzene is 0.224.

Assuming a loading of  $1.8 \text{ mg/cm}^2$  of dirt on the skin,  $1980 \text{ cm}^2$  of skin in contact with soil for an adult and  $1580 \text{ cm}^2$  for a child<sup>18</sup>, 10 % absorption and concentrations of 0.06 to  $2 \text{ ng/g}$  (see s. 3.2.3), leads to an average dermal absorption of  $< 0.1 \text{ ng/d}$  for both adults and children.

### 3.2.4.3 From Benzene Vapour in the Air

The absorption through the skin of vapors in the air can be calculated from the formula<sup>9</sup>:

$$DA_{\text{der}} = K_p \cdot C_a \cdot t_{\text{exp}}$$

where

- $DA_{\text{der}}$  is the absorbed dose per event ( $\text{mg/cm}^2\text{-event}$ )
- $K_p$  is the permeability constant ( $\text{cm/hr}$ )
- $C_a$  is the concentration of the vapor in air ( $\text{mg/cm}^3$ )
- $t_{\text{exp}}$  is the exposure time ( $\text{hr/event}$ )

Two values are given for the permeability coefficient for benzene -  $0.08 \text{ cm/hr}$  (table 7-1, in reference 16) and  $0.206$  (table 7-7, in reference 16). The latter value is estimated from fat/air partition coefficients and the first one is measured experimentally.

From the scenarios presented in section 3.1.2, a reasonable range in weighted air concentrations is 3.5 to  $8 \text{ ug/m}^3$ . The median surface area for an adult is  $1.94 \text{ m}^2$  and for a child,  $0.73 \text{ m}^2$ . The exposure time is 24 hrs.

Using the minimum and maximum values of the concentrations (ie. maximum is taken here as the 90th percentile for concentrations) and the permeability coefficient of  $0.08 \text{ cm/hr}$ , the dose absorbed per day are:

adult : 0.13 to  $0.3 \text{ ug/day}$   
child: 0.05 to  $0.1 \text{ ug/day}$

## 4. RISK CHARACTERIZATION AND PERSPECTIVES

Exposures, expressed as daily intakes in units of  $\text{ug/day}$ , were assessed in section 3. Inhalation, ingestion and dermal routes of exposure were considered. Table 5 below summarizes the daily intakes (or ranges of daily intakes) of benzene, for adults and children, estimated in section 3. It should be noted that in section 3, the intakes for inhalation and sometimes for ingestion assumed 100% bioavailability. The intake for dermal exposures are amounts absorbed systemically and hence already include bioavailability considerations. Table 5 has two columns for both adults and children. The first set of columns (ie. '100 % Bioav') give the intakes with 100 % bioavailability having been assumed; the second set (ie. 'Bioav. Incl. '), gives intakes for which bioavailability has been taken into consideration (ie. if information was available as noted in the footnotes). This second set of columns should give a better picture of the relative importance of various exposure routes. As far as comparison to exposure guidelines and intakes associated with cancer risk, the intakes in the first set of columns of Table 5 will be used since the exposure guidelines are also expressed as intakes for which we have assumed 100 % bioavailability.

To characterize risks, the various exposure guidelines discussed in Section 2 are compared to the estimated exposures from inhalation and other routes as discussed in Section 3. Because of the assumptions, uncertainties and ranges of values available from both exposures (see Table 5) and the various exposure guidelines (see Table 1), risk characterization is most appropriately done by comparison of ranges of values.

Table 6 below provides a graphic representation of this comparison of exposures, exposure guidelines and intakes associated with inhalation cancer risk, based on ug intake/day (ie. 'INTAKE in Micrograms per day' increasing upwards on the vertical scale).

The middle section of Table 6, "Exposures", depicts the exposures calculated in Section 3, expressed as intake/day (ie. ug/day). The exposures depicted are: *Outdoor Air Quality* - the exposure from spending 100 % of the day outdoors; *Typical Outdoor Exposure* - the exposure from three hours only outdoors, provided for perspective on the contribution to risk solely from contaminants present in outdoor air; *Typical Personal Exposures* - the range of exposures associated with ten different exposure scenarios, combining periods of indoor, outdoor and various microenvironment exposures. Exposure scenarios are included for adults and children, assuming 20 and 5 m<sup>3</sup>/day inhalation rates respectively. For 'outdoor air quality' (ie. 100% outdoor exposure), for 'typical outdoor exposures' (ie. 3 hr), and for the 'typical activity patterns' the ranges shown, bracket the lowest mean to the highest 90th percentile. For perspective purposes, the exposures of smokers, directly from smoking activity is also depicted in this section.

The left section of Table 6, "Exposure Guidelines", expresses the various guidelines discussed in Section 2 in terms of calculated "allowable" intake/day for adults and children. The values are taken from Table 1. Within each type of guideline group (eg. outdoor air) ranges of exposure guidelines, when available, are indicated. Thus, ranges of Air Quality Guidelines (ie. 'Outdoor Air'), Occupational guidelines (ie. 'Workplace Air'), and a chronic health effects based reference concentration (ie. 'Chronic AEL'; only one available) are shown. Comparison of "Exposure Guidelines" to "Exposures" should be done with care. For example, occupational guidelines are included for perspective purposes only. For caveats regarding this comparison see section 4.1.1 of the main report.

The right section of Table 6, "Intakes Associated With Cancer Risk", shows the intakes associated with different levels of cancer risk. Ranges of carcinogenic risk levels (associated with  $1 \times 10^{-5}$  risk and  $1 \times 10^{-6}$  risk) are depicted. Comparison of "Exposures" to "Intakes Associated With Cancer Risk" is appropriate for adult exposures only, since cancer risk estimates apply to a lifetime of exposure and people are adults for the majority of their lives. Adult exposures in the bars of the "Exposure" section fall in the top 70 % of the bars which represent exposures of adults and children.

Based on the tabular analysis (Table 5) and the graphic risk characterization (Table 6), the following observations and deductions can be made:

#### Health Messages:

1) It is apparent, that the inhalation route dominates all other exposure routes for benzene. Exposure by ingestion and via absorption across the skin are considerably less and are approximately equal in importance.

2) For a non smoker, inhalation in various microenvironments and outdoors is the main source of exposure to benzene.

3) All the inhalation exposures are less than the chronic acceptable exposure level - 'Chronic AEL (CA)'- (ie. 1400 ug/day from Table 1;) proposed by California (CDHS). This chronic acceptable exposure level

is considered to be purely health based and is protective against all chronic health effects other than cancer risk. Therefore, the possibility of long-term health effects, other than cancer risk is unlikely.

This comparison of exposures to chronic acceptable exposure levels can also be expressed more quantitatively in the form of a hazard index. These hazard index comparisons for all substances are summarized and are found in section 4.1.5 of the main report.

Table 5. Summary of Estimated Daily Intakes and/or Range of Intakes (in ug /day), from Various Exposure Pathways (ie. intakes, assuming 100 % bioavailability and intakes with bioavailability taken into consideration)

EXPOSURE PATHWAY		ADULT ug/day  (100 % Bioav.)	ADULT ug/day  (Bioav. Incl.)	CHILD ug/day  (100 % Bioav.)	CHILD ug/day  (Bioav. Incl.)
INHALATION	Outdoor Air Quality - Windsor (ie. 100 % outdoor exposure)(a)	60.4 - 111.4	30 - 56 (f)	15.1 - 27.9	7.6 - 14 (f)
	Typical outdoor exposure (ie. ~ 3hr)(b)	7.6 - 13.9	3.8 - 7 (f)	1.9 - 3.5	1 - 1.8 (f)
	Typical personal exposures(ie. Table 4) (c)	67.2 - 339.5	34 - 170 (f)	17.4 - 39.2	8.7 - 20 (f)
	Smoking (e)	1125 - 2305	563 - 1175 (f)		
INGESTION	Food (d)	0.02 - 2	0.02 - 1.8	0.02 - 2	0.02 - 1.8
	Drinking water (d)	0.05 - 0.09	0.05 - 0.08	0.03 - 0.05	0.03 - 0.05
	Soil (d)	0.00004	0.00004	0.00016	0.0001
	TOTAL (Ingestion)	0.07 - 2.1	0.07 - 1.9	0.05 - 2.1	0.05 - 1.9
DERMAL	During showering		0.05 - 0.07		0.02 - 0.03
	Contact with soil & dirt		<0.0001		<0.0001
	From benzene vapour in the air		0.1 - 0.3		0.05 - 0.01
	TOTAL (Dermal)		0.2 - 0.4		0.07 - 0.04

a.) Range of intakes is associated with the range of the 'mean' to '90th percentile' concentrations in outdoor air. It is to be noted that people are not exposed 24 hours to outdoor air. This estimation assumes 100 % exposure to outdoor air and is a measure of outdoor air quality per se and not of actual exposure.

b.) Range of intakes calculated from the 'mean' to '90th percentile' concentrations in outdoor air and assuming a 'typical' outdoor air exposure of = 3 hr (ie. corresponding to breathing 2.5 m<sup>3</sup>/hr for adults and 0.63 m<sup>3</sup>/hr for children).

c.) Range of intakes is estimated from the range of the lowest 'mean' and the highest '90th percentile' concentrations obtained from personal exposure and microenvironment measurements.

d.) The absorption rate is taken as 90% (s 1.1)

e.) The intake shown is the direct intake (ie. from average to upper bound estimate) of an adult smoker from smoking activity (ie. 'smoking') only. Various smoking environments for adults and children have already been included in the 'typical personal exposure' scenarios.

f.) The absorption rate is 50% (see s 1.1).

4) The most conservative range of available exposure guidelines are depicted in Table 6 under Intakes Associated with Cancer Risk. These guidelines were proposed by CDHS, the US EPA, and the World Health Organization. As shown in Table 6, they are exceeded by the estimated exposures. Because people are adults for the majority of their lives, these intakes associated with cancer risk are depicted for adults only. The inhalation intakes for adults associated with 'outdoor air quality' (ie. 100 % outdoor exposure), 'typical outdoor exposure' (ie. 3 hr) and 'typical personal exposures' range between 60 - 111 ug/day, 8 - 14 ug/day and 67 - 340 ug/day, respectively (from Tables 2, 4 and 5). These intakes and the corresponding doses in mg/kg-day are summarized in Table 7. Using the various potencies from the three agencies, the range of risks associated with 'outdoor air quality' (ie. 100% outdoor exposure) is between  $1.2 \times 10^{-5}$  and  $1.6 \times 10^{-4}$ . Similarly the range of risks associated with 'typical outdoor exposures' (ie. 3 hr) is between  $1.5 \times 10^{-6}$  and  $2.0 \times 10^{-5}$ . Similarly the range of risks associated with 'typical personal exposures' is between  $1.3 \times 10^{-5}$  and  $4.9 \times 10^{-4}$ . The risks associated with 'typical personal exposures' are slightly higher than the risks associated with 'outdoor air quality' which in turn is higher than 'typical outdoor exposures'. This range of risk analysis is summarized in Table 7. It should be further noted, that this risk characterization (ie. using carcinogenic risk based limits) is based on an assumed lifetime exposure (ie. 24 hours, every day, for 70 years) and hence is a very conservative assumption.

5) The exposure that a smoker experiences is considerably higher than any of the exposures associated with 'personal activity patterns', 'outdoor air quality' and 'typical outdoor exposures'.

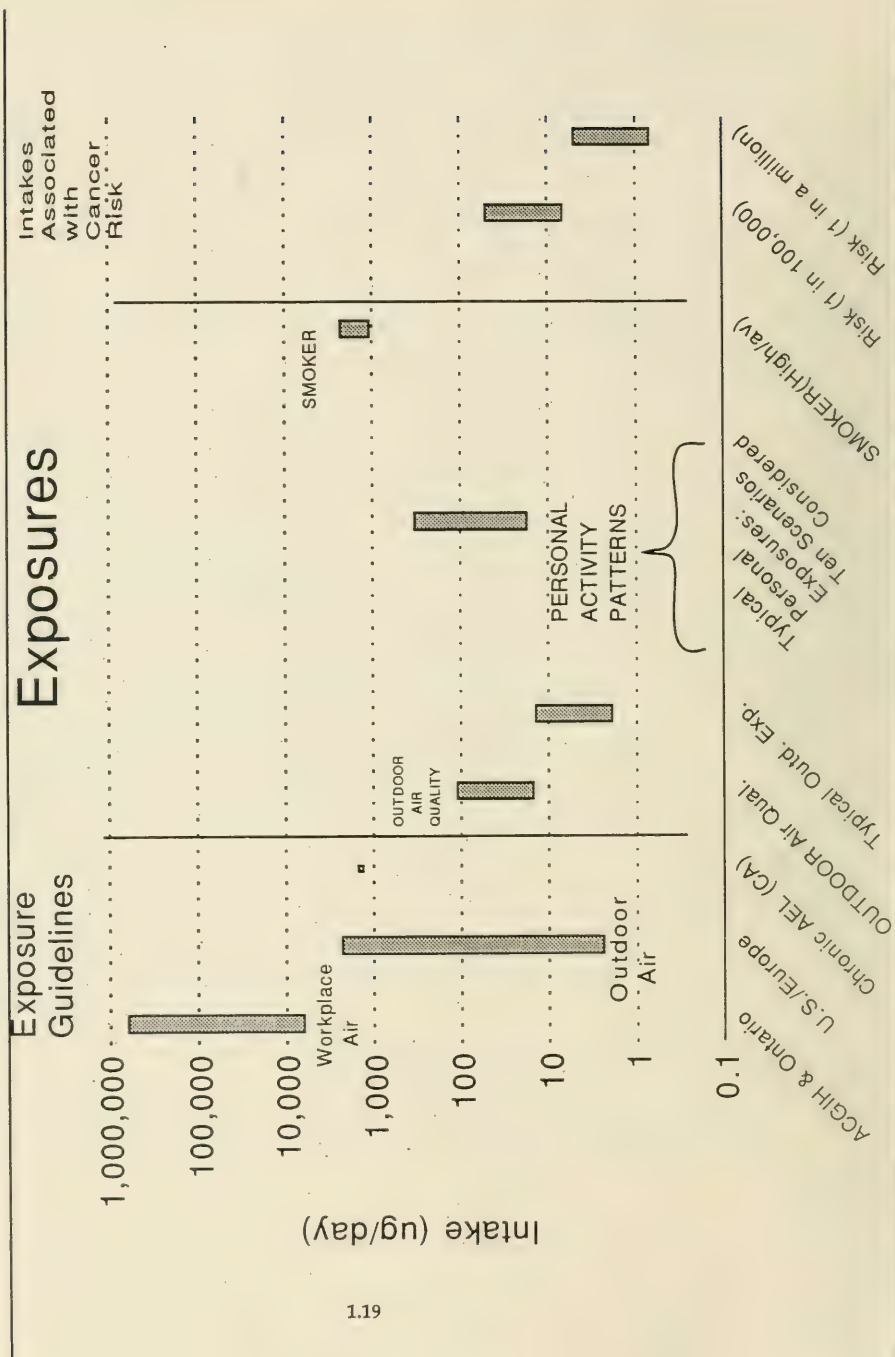
6) For a smoker, the inhalation exposure is dominated by the benzene in cigarettes. Adding an additional exposure of 80 ug/day from air to the 1125 ug/day from cigarettes leads to an average total intake of 1205 ug/day. As noted previously, the maximum intake could be as high as 2305 ug/day (ie., for high tar cigarettes). The average to high intakes correspond to doses of 0.017 to 0.034 mg/kg-day. The corresponding risks for the average intake are  $5 \times 10^{-4}$  (EPA) or  $1.7 \times 10^{-3}$  (CDHS) and for the high intake (ie., high tar)  $1 \times 10^{-3}$  (EPA) or  $3.4 \times 10^{-3}$  (CDHS).

7) The inhalation during showering adds on  $7 \times 10^{-6}$  mg/kg-day to the inhalation exposure. This is considered insignificant when compared to the exposure contributed by other activity patterns.



Table 6. BENZENE RISK CHARACTERIZATION in WINDSOR  
 Ranges of exposure guidelines, exposures and risk estimates  
 (Inhalation unless otherwise specified)

4C4



**Table 7. Range of Inhalation Cancer Risks Associated with Estimated Intakes (ie. for adult exposures only) of Benzene**

RANGE of INHALATION INTAKES			POTENCY (a)		RANGE of RISKS
Environment	Unit ug/day	Unit mg/kg/day	Agency	Unit (mg/kg-d) <sup>-1</sup>	
OUTDOOR AIR QUALITY (Windsor)	60 - 111	8.6 x 10 <sup>-4</sup> - 1.6 x 10 <sup>-3</sup>	EPA	2.9 x 10 <sup>-2</sup>	2.5 x 10 <sup>-5</sup> - 4.6 x 10 <sup>-5</sup>
			CDHS	0.1	9.0 x 10 <sup>-5</sup> - 1.6 x 10 <sup>-4</sup>
			WHO	1.4 x 10 <sup>-2</sup>	1.2 x 10 <sup>-5</sup> - 2.2 x 10 <sup>-5</sup>
			OVERALL RANGE OF RISKS: 1.2 x 10 <sup>-5</sup> - 1.6 x 10 <sup>-4</sup>		
TYPICAL OUTDOOR EXPOSURE (ie.= 3 hr.)	8 - 14	1.1 x 10 <sup>-4</sup> - 2.0 x 10 <sup>-4</sup>	EPA	2.9 x 10 <sup>-2</sup>	3.2 x 10 <sup>-4</sup> - 5.8 x 10 <sup>-4</sup>
			CDHS	0.1	1.1 x 10 <sup>-5</sup> - 2.0 x 10 <sup>-5</sup>
			WHO	1.4 x 10 <sup>-2</sup>	1.5 x 10 <sup>-6</sup> - 2.8 x 10 <sup>-6</sup>
			OVERALL RANGE OF RISKS: 1.5 x 10 <sup>-6</sup> - 2.0 x 10 <sup>-5</sup>		
TYPICAL PERSONAL EXPOSURES	67 - 340	9.6 x 10 <sup>-4</sup> - 4.9 x 10 <sup>-3</sup>	EPA	2.9 x 10 <sup>-2</sup>	8.0 x 10 <sup>-5</sup> - 1.4 x 10 <sup>-4</sup>
			CDHS	0.1	9.6 x 10 <sup>-5</sup> - 4.9 x 10 <sup>-4</sup>
			WHO	1.4 x 10 <sup>-2</sup>	1.3 x 10 <sup>-5</sup> - 6.9 x 10 <sup>-5</sup>
			OVERALL RANGE OF RISKS: 1.3 x 10 <sup>-5</sup> - 4.9 x 10 <sup>-4</sup>		
a. These are equivalent potency factors calculated from the unit risks proposed by the agencies listed; assumed adult weight of 70 kg and 20 m <sup>3</sup> per day.					

8) Considering the information in Table 5, the exposures from the *non-inhalation* pathways are:

- *Ingestion* of food, water and soil:

adult - 0.07 to 1.9 ug/day

child - 0.05 to 1.9 ug.day

- *Dermal* absorption:

During showering and bathing and from soil and dirt:

adult: 0.05 to 0.07 ug/d; child: 0.02 - 0.03 ug/d;

From benzene vapour in the air: adult - 0.1 to 0.3 ug/day

child - 0.05 to 0.01 ug/d

These ingestion and dermal exposures are = 10 to over 1000 times less than from inhalation and therefore do not add significantly to the cancer risk from exposure to benzene.

**Regulatory compliance messages:**

9) The risk characterization in Table 6 indicates that, for the inhalation receptor exposures considered:

- The exposures potentially associated with outdoor air quality, for adults, youth and children, fall in the lower 5% range of the air quality guidelines of various jurisdictions.
- Exposures associated with typical outdoor exposure (ie.3 hr) fall in the lower 1 % range of the air quality guidelines of various jurisdictions
- Exposures associated with personal activity patterns fall in the lower 15% range of the air quality guidelines of various jurisdictions.

It should be noted that these air quality guidelines may be of different types. Some are purely health based and some are regulatory and therefore may have been influenced by various risk management considerations. The regulatory guidelines may also have different uses (eg. judging the acceptability of air quality per se or judging the incremental addition by a source to the existing air quality).

10) Table 6 also indicates that all the inhalation exposures are less than the range of occupational levels.

11) The ingestion intake is also much lower than the US EPA ten-day health advisory of 235 ug/L for a 10 kg child drinking 1 L/day. This health advisory is not valid for lifetime exposures.

12) The MOEE maximum allowable concentration for drinking water of 5 ug/L is equivalent to an allowable intake via ingestion of 7.5 ug/d ( $1 \times 10^{-4}$  mg/kg-day) for an adult or 3.8 ug/d ( $2.4 \times 10^{-4}$  mg/kg-day) for a child. The actual ingestion is below this amount.

13) MOEE is presently reviewing benzene for the purposes of standard setting.

#### Summary and recommendations:

- ♦ All the inhalation exposures are less than the chronic acceptable exposure level and therefore, the possibility of long-term health effects, other than cancer risk, is unlikely.
- ♦ The range of estimated inhalation risks associated with 'outdoor air quality' (ie. 100% outdoor exposure) is between  $1.2 \times 10^{-5}$  and  $1.6 \times 10^{-4}$ . Similarly the range of risks associated with 'typical personal exposures' is between  $1.3 \times 10^{-5}$  and  $4.9 \times 10^{-4}$ . Since these levels of risks exceed  $1 \times 10^{-5}$ , a level generally deemed to be negligible, it is recommended that benzene be considered a candidate for reduction of exposure.
- ♦ Exposures and therefore risks associated with 'typical personal exposures' are slightly higher than the risks associated with 'outdoor air quality'.
- ♦ The commuting and tobacco smoke-affected environments are the most dominant in the upper range of 'typical personal exposures'.
- ♦ The exposure that a smoker experiences is considerably higher (ie. associated risks are between  $5 \times 10^{-4}$  and  $3.4 \times 10^{-3}$ ) than the exposures associated with 'personal activity patterns' and 'outdoor air quality'.
- ♦ Ingestion and dermal exposures are  $\approx 10$  to over 1000 times less than from inhalation and therefore do not add significantly to the cancer risk from exposure to benzene.

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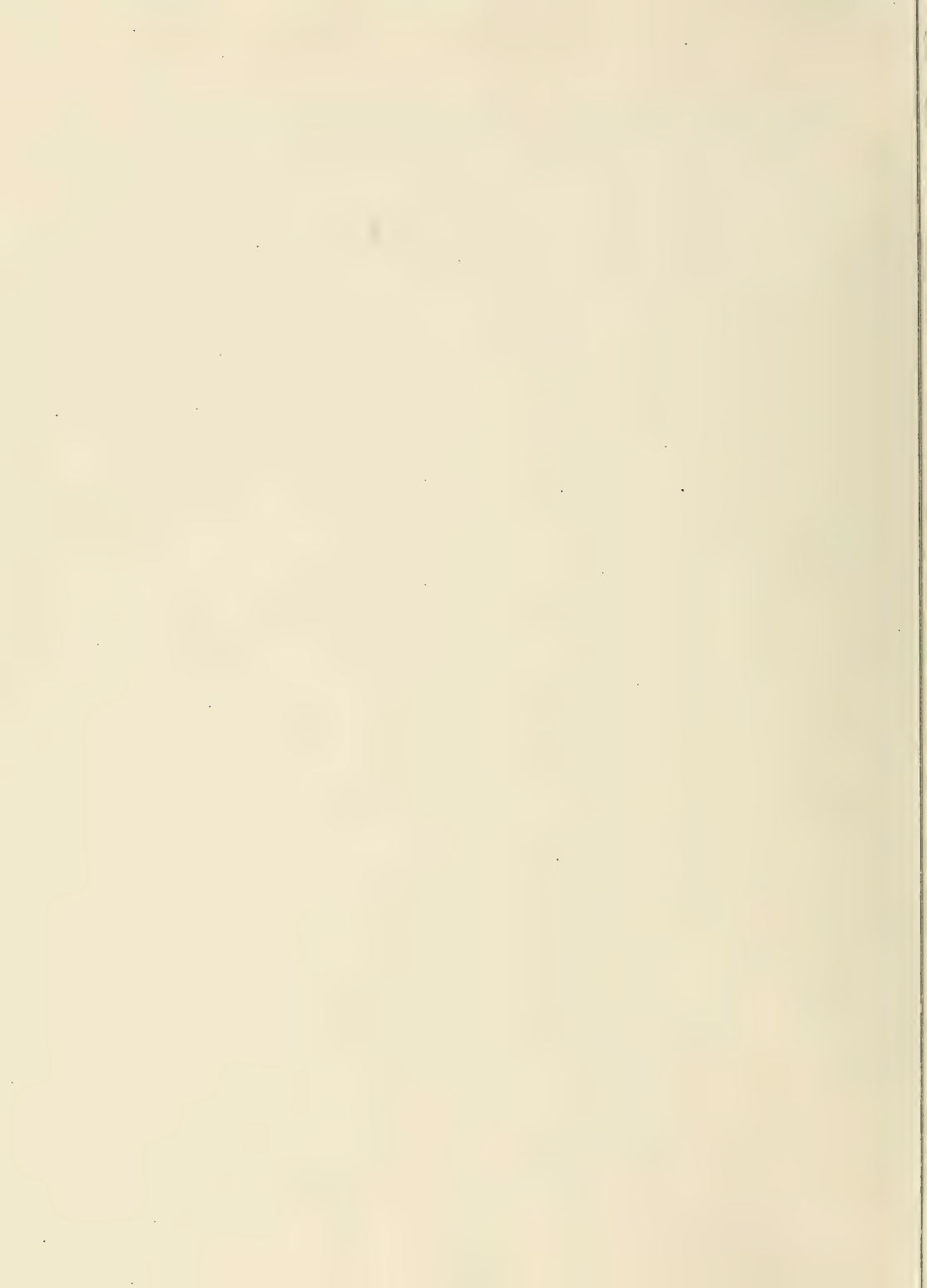
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## APPENDIX 2

### RISK ANALYSIS FOR 1,3 - BUTADIENE



## APPENDIX 2

### RISK ANALYSIS FOR 1,3 - BUTADIENE

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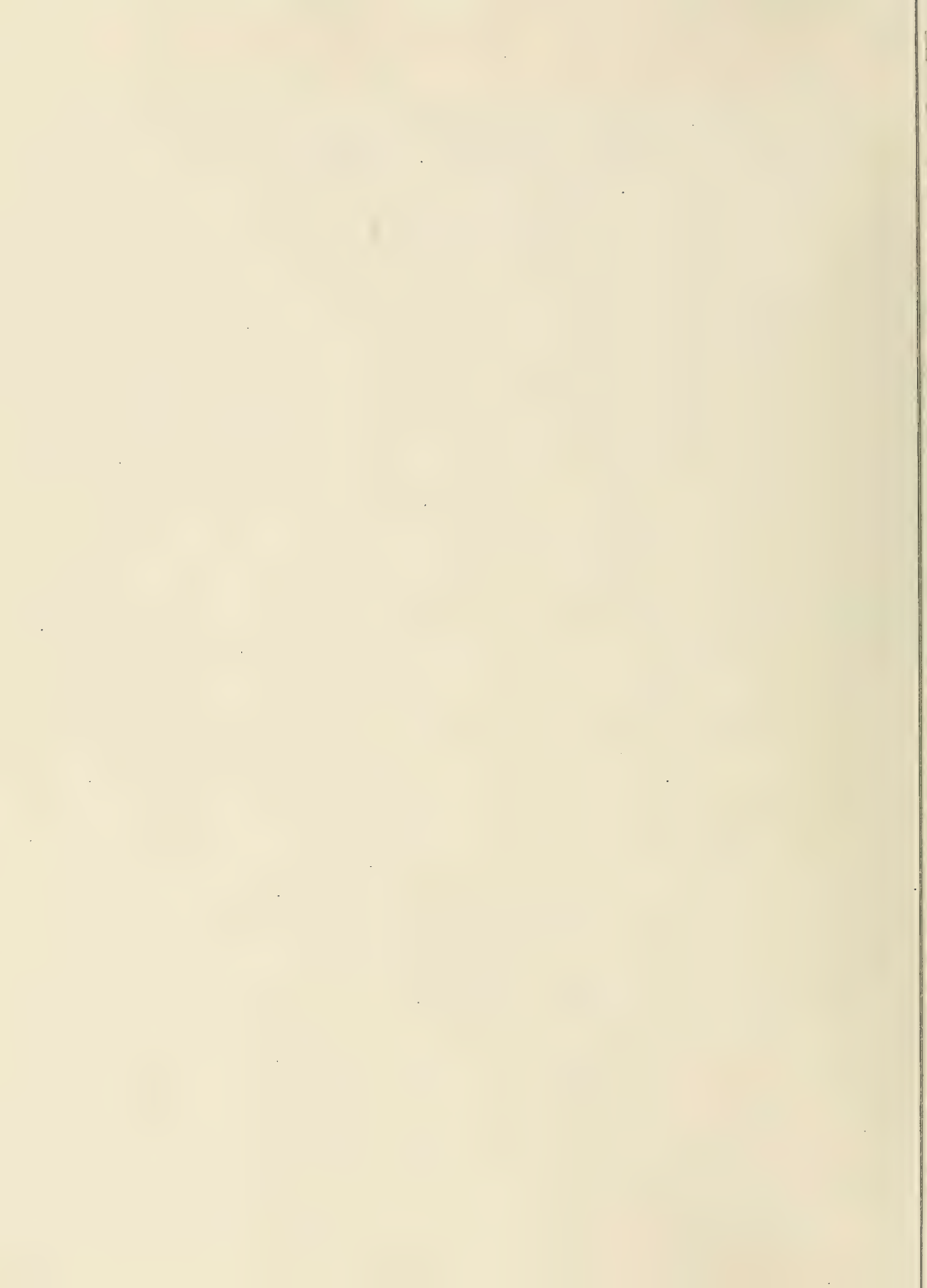
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## 1,3 - BUTADIENE

### DESCRIPTION and SOURCES of 1,3 - BUTADIENE.

1,3 - Butadiene is a colorless, flammable gas with an odour resembling gasoline. Very large amounts are produced every year from petroleum. It is used to make rubber for car and truck tires and also other kinds of rubber and plastics. 1,3 - butadiene may be present in small amounts in gasoline.

1,3 - Butadiene enters the environment during production, storage, transport, venting and combustion of gasoline. Gasoline vapours but primarily the exhaust of automobiles and trucks are sources of 1,3 - butadiene. Other sources are petroleum refineries, chemical, rubber and plastic manufacturing plants, and smoke from wood fires, burning of plastics and cigarettes. It is always present in the air around cities and towns at low levels. In 1987, an estimated total of 9 million pounds were released to the atmosphere from manufacturing and processing facilities in the U.S.

### 1. HAZARD IDENTIFICATION

#### 1.1 Absorption and Metabolism

1,3-Butadiene is a gas at ambient temperature and pressure and, as such, exposure of individuals occurs mainly through inhalation of contaminated air. The pulmonary absorption is considered rapid as suggested by a blood/air partition coefficient of 0.60-0.65, and to occur by passive diffusion at the alveolar/epithelial interface<sup>1</sup>. In its Integrated Risk Information System (IRIS)<sup>2</sup>, the US EPA suggests a 20% absorption rate at low exposure levels. On the other hand, little information is available on the bioavailability of 1,3-butadiene by the gastrointestinal and dermal routes. The latter could be regarded as significant in view of the lipophilic nature of the chemical ( $pK_{ow} \approx 2$ )<sup>1</sup>.

Systemic distribution of 1,3-butadiene occurs rapidly following pulmonary absorption, with major amounts being directed to perinephric fat, brain, liver, and kidney<sup>1</sup>. Metabolism occurs mainly in the liver by the mixed-function oxidase (cytochrome P-450) complex and results in reactive epoxides and diols<sup>3</sup>. These are presumed to be responsible for the genotoxicity and systemic effects of 1,3-butadiene<sup>4</sup>. Although a comprehensive identification of all of the 1,3-butadiene metabolites has not been performed yet, the primary pathway is thought to proceed first through the formation of 1,2-epoxybutene-3, with subsequent transformations into diepoxybutane, 3-butene-1,2 diol, and 3,4-epoxy-1,2-butane diol<sup>1,3</sup>. Significant differences have been reported in the capacity of experimental animals to handle 1,3 -butadiene<sup>3</sup>. Generally, mice are metabolically more active than rats, a phenomenon that may be partly responsible for their higher susceptibility to 1,3 - butadiene-induced systemic effects and cancer<sup>6,7</sup>. The implications of these interspecies differences for the estimation of human health risk, however, are uncertain.

1,3-butadiene and its metabolites are mainly excreted in urine following inhalation exposure, with smaller amounts being found in expired air and feces<sup>1</sup>. The elimination is rapid, with 77%-99% of the initial tissue amount being cleared with half-lives of between 2 and 10 hours<sup>1</sup>.

#### 1.2 Toxicology

The systemic effects produced by 1,3-butadiene and its metabolites on biological systems are numerous. Studies in animals have demonstrated the capacity of these compounds to induce disturbances of the respiratory, cardiovascular, hepatic, renal, gastrointestinal, hematological, immunological, and neurological systems<sup>1</sup>. Furthermore, these compounds have been shown to possess genotoxic activity and to induce developmental and reproductive effects. Few of these systemic effects however have been observed in humans. Only cases of reversible hematological disorders, resulting in slightly decreased levels of red

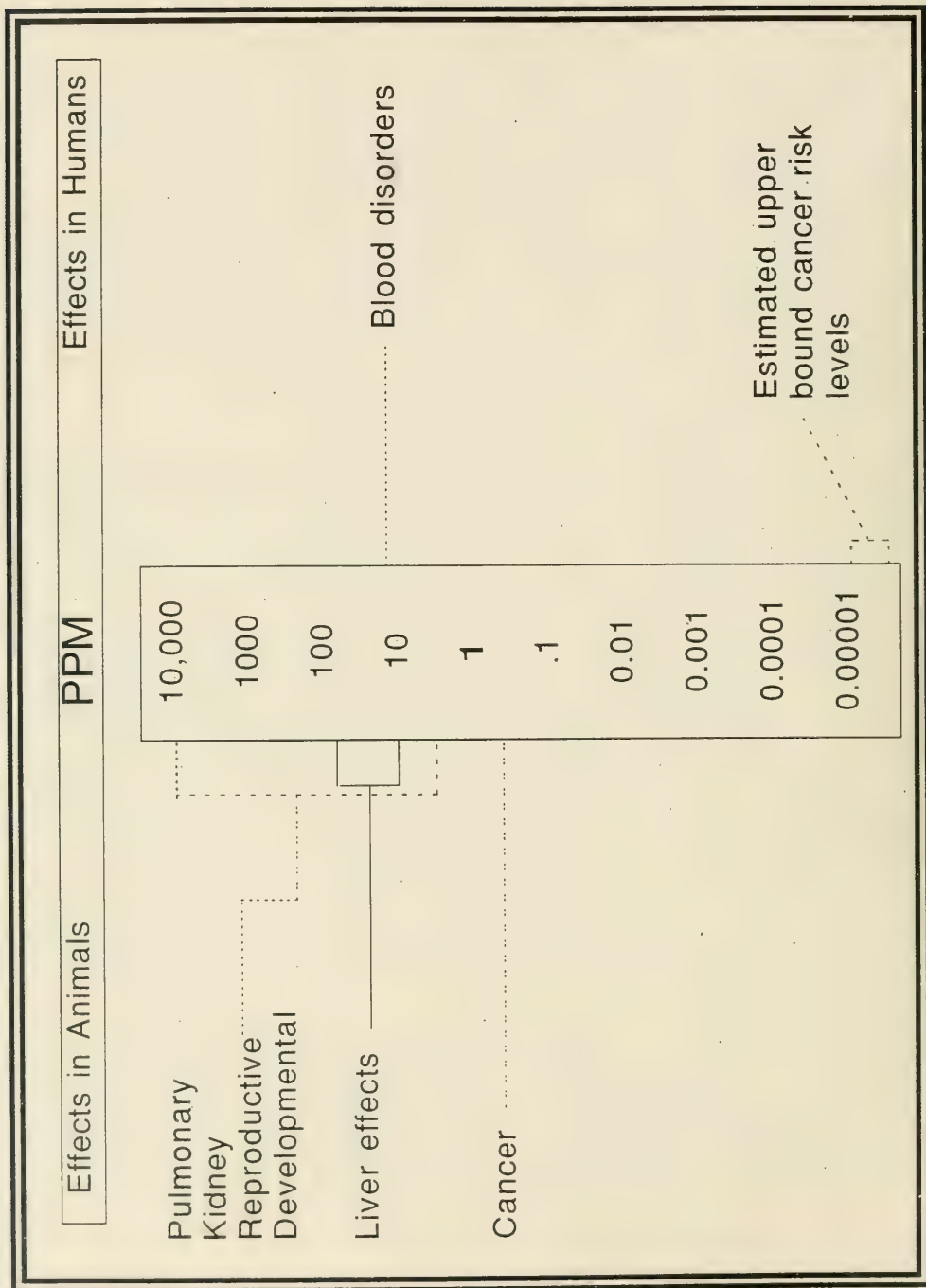


Figure 1.1 Summary of chronic effects associated with the inhalation of various concentrations of 1,3-butadiene (adapted from 9)(1ppm corresponds to 2.21 mg/m³)

blood cells, hemoglobin, platelets, and neutrophils, seems to have been documented following chronic exposure<sup>1</sup>. In general, these effects occur following exposure to occupational-like concentrations of 1,3-butadiene (Figure 1.1), a situation which is considered of little relevance to the general population. In fact, a recent study estimates that ambient levels of 1,3-butadiene in major US centers oscillate around 0.00045 ppm (1  $\mu\text{g}/\text{m}^3$ )<sup>5</sup>. These levels are almost 50,000 times lower than the concentrations associated with reversible blood effects in exposed workers (20 ppm)<sup>1</sup>. Similarly, chronic exposure of female mice to 20 ppm of 1,3-butadiene resulted in reproductive effects<sup>1</sup>, a class of afflictions considered highly relevant for environmentally exposed populations. However, although a NOAEL was not reported in this study, these levels are, once again, approximately 50,000 higher than the average ambient air concentration of 1,3-butadiene. For Windsor, this ratio is even higher, since average ambient levels of 1,3-butadiene were  $\approx 0.2 \mu\text{g}/\text{m}^3$  (see Table 2).

1,3-butadiene has been tested for genotoxicity in a number of *in vitro* and *in vivo* systems<sup>1,4,8</sup>. Positive results were reported in certain strains of *Salmonella typhimurium* in the presence of metabolic activation, and in the *in vivo* induction of micronuclei, chromosomal aberrations, sister chromatid exchange, and dominant lethal assay in mice. These observations have not been reproduced in humans who seem, among other factors, to be less active metabolically than rodents<sup>4</sup>.

The only consistent finding that has been observed in both animals and humans is the occurrence of malignancies following inhalation exposure to occupational concentrations of 1,3-butadiene<sup>1</sup>. Epidemiological retrospective studies of mortality among workers in the synthetic rubber industry and 1,3-butadiene monomer producing industry were conducted by several investigators and were reviewed recently<sup>9,10</sup>. Some of these studies have reported increased mortality associated with stomach, lymphatic and hematopoietic cancers (leukemia, Hodgkin's disease, lymphosarcoma). The specificity of the exposure in these various studies, however, is unclear in view of the possible contribution from other chemicals to the total exposure experienced by these cohorts<sup>9,10</sup>. Furthermore, Ott<sup>9</sup> reported that there were no remarkable mortality findings relative to the cancer sites examined for three cohorts viewed together, although it is noteworthy that this approach of combining different cohorts may not be appropriate in all cases. It has been suggested, therefore, that these studies do not provide convincing evidence that links adverse mortality effects to 1,3-butadiene exposure<sup>9</sup>. In fact, in 1990 Landrigan<sup>10</sup> noted that "...none of the epidemiological studies currently available has developed sufficient information on exposure to permit description of a quantitative dose-response relationship or to serve as a basis for quantitative estimation of risk<sup>10</sup>. In view of this situation, which still prevails today<sup>11</sup>, the animal database has traditionally been used for the projection of human health risk to 1,3-butadiene.

Results from long-term, chronic studies in mice and rats have clearly demonstrated the carcinogenic potential of 1,3-butadiene<sup>1,6,7,11</sup>. In the more recent chronic inhalation studies conducted in mice by the National Toxicology Program (NTP)<sup>11</sup>, various neoplastic changes were observed, including hemangiosarcomas of the heart, thymic lymphoma, and alveolar-bronchiolar neoplasms. Lung neoplasms in female mice were increased in all exposure groups, including the low-dose group of 6.25 ppm 1,3-butadiene. It is interesting to note that this exposure concentration is comparable to some current occupational exposure limit such as the ACGIH<sup>12</sup> TLV-TWA of 10 ppm and the proposed OSHA standard of 2 ppm<sup>11</sup>. Based on these new results, a major revision of the 1,3-butadiene air guidelines/standards is underway by several regulatory agencies.

Based on the carcinogenic profile of 1,3-butadiene observed in animals and humans, this compound has been classified as a "Probable Human Carcinogen" (B2) by the US EPA, and was recently reviewed to "Probably Carcinogenic to Humans" (2A) by the International Agency for Research on Cancer (IARC)<sup>5</sup>.

## 2. DOSE-RESPONSE INFORMATION/CURRENT EXPOSURE GUIDELINES



The uncertainties surrounding the potential toxicological effects of environmental 1,3-butadiene on communities have influenced the methodologies used to set guidelines and permissible exposure levels. As noted previously, the adoption of reasonably conservative assumptions is warranted in this context in order to provide sufficient protection of public health. This section summarizes various health criteria values, that is, exposure guidelines and dose-response information that leading regulatory agencies (and other relevant sources) have proposed and consider appropriate for permitting, assessing, and characterizing risks associated with various exposures. Potential exposures to 1,3-butadiene are evaluated in section 3 and the risk characterization is presented in section 4.

## 2.1 Air Guidelines

### 2.1.1 Chronic, Non-Carcinogenic Health Effects

The US EPA's Integrated Risk Information System database (IRIS)<sup>2</sup> notes that the inhalation Reference Concentration (RfC) for 1,3-butadiene is not available at this time. EPA defines an RfC as an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime.

No inhalation chronic AEL (Acceptable Exposure Level), nor AGC (Annual Guideline Concentration) have been proposed for 1,3-butadiene by The California Department of Health Services<sup>14</sup> and by the New York State Department of Environmental Conservation<sup>15</sup>, respectively.

A TEL (Threshold Effect Exposure Limit) of 1.2  $\mu\text{g}/\text{m}^3$  based on occupational exposure guidelines was derived by the Massachusetts Department of Environmental Protection<sup>16</sup>.

Generally, the inhalation chronic AEL, TEL, and the inhalation RfC noted above are comparable in their use for assessing chronic effects (except carcinogenic effects) due to inhalation. As noted previously, it is expected that constraining environmental exposures of human populations to cancer-preventive levels of 1,3-butadiene should decrease to negligible levels, or simply eliminate depending on the end-point of concern, the probability of occurrence of chronic non-cancer health effects.

### 2.1.2 Carcinogenic effects

For the purpose of estimating cancer risk, the U.S. EPA<sup>2</sup> has established an inhalation unit risk of  $2.8 \times 10^{-4} (\text{ug}/\text{m}^3)^{-1}$  for continuous lifetime exposure to 1  $\text{ug}/\text{m}^3$  of 1,3-butadiene. In other words, an estimated lifetime risk of  $1/10^6$  of contracting cancer in this particular case would be associated with a lifetime average daily exposure (LADE) to 0.0036  $\text{ug}/\text{m}^3$ . No quantitative estimate of carcinogenic risk from oral exposure (*i.e.*, oral cancer potency factor,) is proposed as 1,3-butadiene is a gas at room temperature and pressure, making oral exposure unlikely. The U.S. EPA unit risk estimate was based on a 1984 NTP bioassay, and is a geometric mean of the unit risks obtained from inhalation studies in male and female mice exposed to relatively high concentration of 1,3-butadiene (0, 650, 1250 ppm). The linearized multistage model (extra risk) was used to extrapolate a 95% UCL (upper confidence limit) on a projected risk of  $1/10^6$ . Recent studies, however, have demonstrated the capacity of 1,3-butadiene to induce significant incidences of lung neoplasms in female mice chronically exposed to concentrations as low as 6.25 ppm (see Section 1.2). Furthermore, new data that would allow a more realistic evaluation of the pharmacokinetics of 1,3-butadiene in mammals has become available. As a result, a major revision of the current unit risk factor is presently underway by the US EPA and other agencies<sup>5</sup> and, therefore, the current value should be considered provisional.

The following US state agencies have adopted the US EPA inhalation unit risk factor for the development

of an annual-based value: the Massachusetts Department of Environmental Protection (MDEP)<sup>16</sup>, the New York State Department of Environmental Conservation (NYSDEC)<sup>15</sup>, and the Michigan Department of Environmental Conservation (MDEC)<sup>1</sup>. Other jurisdictions may have based their methodologies on the US EPA unit risk factor although their final air guidelines differ substantially from those proposed by the agencies above mentioned. Therefore, judging the applicability of these guidelines for the current work is difficult as little information was provided on the factors affecting the computation<sup>1</sup>.

The California Department of Health Services (CDHS) established a unit risk factor of  $1.7 \times 10^{-4} \text{ (ug/m}^3\text{)}^{-1}$ , based on the most recent NTP mouse inhalation studies<sup>7,11</sup> whose results were fitted to the linearized multistage model<sup>5</sup>.

The Occupational Safety and Health Administration (OSHA) also developed unit risk values for 1,3-butadiene using both pooled tumor and site-specific tumor incidence data for both mice and rats based mainly on the 1984 NTP bioassay. The unit risk values obtained using the multistage model ranged from  $2.7 \times 10^{-6} \text{ (ug/m}^3\text{)}^{-1}$  to  $7.5 \times 10^{-6} \text{ (ug/m}^3\text{)}^{-1}$  depending on the end-points retained<sup>5</sup>. For the present risk assessment, the unit risk factor of  $7.5 \times 10^{-6} \text{ (ug/m}^3\text{)}^{-1}$  (most conservative) was retained in view of the uncertainties surrounding the relevance of animal end-points for humans, and considering that future estimates of risk may change as a result of the current review of the 1,3-butadiene guideline.

No air guidelines for 1,3-butadiene have been suggested by the World Health Organization (WHO) and its subsidiary, the International Agency for Research on Cancer (IARC), although the probable carcinogenicity of this compound in humans has been recognized recently<sup>3</sup>.

In the case of Ontario, no air guidelines are available and new values based on the most recent toxicological information are under development at the Ministry of the Environment and Energy.

Occupational exposure guidelines have been developed for 1,3-butadiene. In the US, the American Conference of Industrial Hygienists (ACGIH)<sup>12</sup> presently has a Threshold Limit Value-Time Weighted Average (TLV-TWA) of 10 ppm (22000 ug/m<sup>3</sup>) which is currently under review in light of the recent reports on animal carcinogenicity at 6.25 ppm<sup>7,11</sup>. The Permissible Exposure Limit (PEL-TWA), established by the Occupational Safety and Health Administration (OSHA)<sup>12</sup> is 1000 ppm (2200 mg/m<sup>3</sup>) although OSHA has proposed to reduce the PEL to 2 ppm (4400 ug/m<sup>3</sup>) as an 8-hour TWA<sup>12</sup>. Occupational exposure limits for Australia and the United Kingdom are 10 ppm in both cases<sup>12</sup>.

The current Ontario occupational guideline for 1,3-butadiene is 10 ppm (22000 ug/m<sup>3</sup>) with a notice of intended change to 1 ppm (2200 ug/m<sup>3</sup>).

The above guidelines for atmospheric 1,3-butadiene are summarized in Table 1 below.

## 2.2 Other Route Guidelines

Exposure of the general population to 1,3-butadiene is expected to be dominated by inhalation in view of the gaseous properties of this chemical<sup>1</sup>. On the other hand, residues of 1,3-butadiene have been detected in certain well waters. They have also been found in rubber and plastic food containers. This suggests that very low-levels exposure to the general population may occur by absorption through the gastrointestinal tract. Furthermore, 1,3-butadiene is a constituent of gasoline, and dermal exposure may occur upon contact during refueling or other uses<sup>1</sup>. These routes, *i.e.*, ingestion and dermal uptake, are not expected to represent significant quantitative pathways of human exposure and, to our knowledge, no studies exist that have investigated toxicological effects following exposure other than by inhalation. Indeed, no information regarding oral potency slope and/or guidelines for dietary or dermal 1,3-butadiene were located in the literature.

TABLE 1. Summary of Exposure Guidelines for 1,3-Butadiene from Leading Agencies

GUIDELINE APPLICATION	AGENCY(IES) (4)	ORIGINAL VALUE	CONCENTRATION ("Original Form" converted to these -as applicable)			CALCULATED "ALLOWABLE" INTAKE (3)
			Unit Risk (1)	RsC (2) (1 x 10 <sup>-4</sup> )	RsC (2) (1 x 10 <sup>-4</sup> )	
INHALATION GUIDELINES						
Occupational	ACGIH, Ontario, OSHA	2200-2200000 ug/m <sup>3</sup>	NA	NA	NA	44,000 - 44,000,000 (0.63 - 628)
Ambient Air Quality Guidelines	US States	0.004-0.04 ug/m <sup>3</sup>	NA	NA	NA	0.08 - 0.8 (1.1 x 10 <sup>-4</sup> - 1.1 x 10 <sup>-3</sup> )
Ontario Air Quality Guideline		NA				
Chronic AELs/RfCs	MDEP	1.2 ug/m <sup>3</sup>	NA	NA	NA	24 (3.4 x 10 <sup>-4</sup> )
Inhalation Cancer Potency Factor	EPA, CDHS, OSHA	See Unit Risk column	2.8 x 10 <sup>-4</sup> 1.7 x 10 <sup>-4</sup> 7.5 x 10 <sup>-4</sup>	0.04 0.06 1.3	0.004 0.006 0.13	for 1 x 10 <sup>-4</sup> risk: 0.8 - 26 (1.1 x 10 <sup>-4</sup> - 3.4 x 10 <sup>-4</sup> ) for 1 x 10 <sup>-4</sup> risk: 0.08 - 2.6 (1.1 x 10 <sup>-4</sup> - 3.4 x 10 <sup>-4</sup> )
INGESTION GUIDELINES						
Drinking Water Guideline	NA					
Oral Cancer Potency Factor	NA					

<sup>1</sup>For inhalation and ingestion guidelines, unit risks are expressed as (ug/m<sup>3</sup>)<sup>-1</sup> and (ug/L)<sup>-1</sup>, respectively<sup>2</sup>For inhalation and ingestion guidelines, risk specific concentrations are expressed as ug/m<sup>3</sup> and ug/L, respectively<sup>3</sup>Intake was computed by assuming, where applicable, an adult weight of 70 kg, a breathing rate of 20 m<sup>3</sup>/day, a water intake of 1.5 L/day. In all cases 100% bioavailability of the intake was assumed.<sup>4</sup>See glossary for agency definitions.

### 3. HUMAN EXPOSURE ASSESSMENT

#### 3.1 Inhalation

##### 3.1.1 Ambient Air Quality

Ambient levels of 1,3 - butadiene have been measured at five fixed site stations in Windsor by two monitoring agencies, the Ontario Ministry of Environment and Energy and the Environmental Protection Service of Environment Canada. For this assessment, data from only three sites were available. The measurement period extends from 1988 to 1991 and includes 253 samples of 24 hour average each. Concentration levels range from non-detectable to 1.38  $\mu\text{g}/\text{m}^3$ , with the median, arithmetic mean (average), 90th percentile and 95th percentile levels being 0.18, 0.20, 0.39 and 0.54  $\mu\text{g}/\text{m}^3$ , respectively<sup>18</sup>.

It is possible to estimate the daily intake of 1,3 - butadiene associated with these measures of Windsor ambient air quality, recognizing that personal exposures/intakes may be quite different as further discussed in section 3.1.2. Table 2 below shows these estimated intakes for two different receptors, i.e., an adult and a child. It should be noted that these intakes were calculated based on 24 hour exposures to ambient air and assume 100% bioavailability by the inhalation route.

Table 2. Estimated Daily Intakes of 1,3-Butadiene Associated With Ambient Air Quality in Windsor

Air Quality Measure (a)	Concentration $\mu\text{g}/\text{m}^3$	Adult (b) $\mu\text{g}/\text{day}$ ( $\mu\text{g}/\text{kg}\cdot\text{day}$ )	Child (b) $\mu\text{g}/\text{day}$ ( $\mu\text{g}/\text{kg}\cdot\text{day}$ )
Median	0.18	3.6 (0.05)	0.9 (0.06)
Mean	0.20	4.0 (0.06)	1.0 (0.07)
90th percentile	0.39	7.8 (0.11)	2.0 (0.13)
<p><sup>a</sup> Based on 253, 24 hour average samples <sup>b</sup> Assuming the following weights and inhalation rates per day (ie. per 24 hour period): Adult: 70 kg; 20 <math>\text{m}^3/\text{day}</math> Child: 15 kg; 5 <math>\text{m}^3/\text{day}</math></p>			

##### 3.1.2 Microenvironments

It is reasonable to assume that the daily 1,3 - butadiene intakes associated with typical personal exposure patterns can be better estimated from various microenvironmental concentrations than from fixed site monitoring data. For the purpose of scoping population exposures, the set of typical receptors in Table 3 below was considered. Examples of the receptor types and/or their characteristics are also included in Table 3. Using 1,3-butadiene concentrations acquired in various microenvironments, either as part of the personal exposure or subsequent microenvironment study in Windsor, it is possible to scope out various typical personal inhalation exposure scenarios for the above receptors. The estimated daily intakes (in  $\mu\text{g}/\text{day}$ ) of these receptors are summarized in Table 4.



Table 3. Receptors With Typical Personal Exposure Patterns

NAME OF RECEPTOR TYPE	CHARACTERISTICS	NAME OF RECEPTOR TYPE	CHARACTERISTICS
Average Office Worker (Non-smoking)	Eg. - Typical office worker (Based on Windsor volunteers and US EPA TEAM study; not smoking at home)	High Outdoor Receptor	Eg. - Construction workers; - Bicycle couriers - Police - Long distance runners
Average Office Worker (Smoker Environment)	Eg. - Typical office worker (Based on Windsor volunteers and US EPA TEAM study; smoking at home)	High Indoor Receptor	Eg. - 'Shut-ins' - Invalids - Elderly, non-mobile
Average Youth	Eg. Special exposures at shopping malls and athletic facilities (pools) in addition to school;	High Commuting Receptor	Eg. - Bus drivers - Taxi drivers - Delivery/ Distribution Services
Average Child (Non-Smoker Home & No Exposure to Tobacco Smoke)	Eg. Similar to average office worker except 'School' replaces 'Office';	Active Receptor # 1	Eg. - 7 hr/week in Bingo Hall or Bar
Average Child (Non-Smoker Home & Typical Exposure to Tobacco Smoke)	Eg. Includes typical times that children may be in proximity to tobacco smoke, outside the home, based on activity pattern studies;		
Average Child (Smoker Home with Exposure to Tobacco Smoke)	Eg. Child living in a house where there is a smoker		

Table 4. Estimated Daily Intakes (ug/day) Associated with Typical Personal Exposures (See footnote 1.)

MICRO ENVIRONMENT	Air Concentration (ug/m <sup>3</sup> ) (h)	Average Office Worker	Average Office Worker	Youth	Average Child	Average Child	High Outdoor Receptor	High Indoor Receptor	High Commuting Receptor
		Non-smoker	Smoker Home Environments		Non smoker home/No exposure to tobacco smoke	Non smoker home/Typical exposure to tobacco smoke			
Office	0.2/1.0 (m)	6.7(a)	6.7(a)				1.7		Time spent (hrs)
School	0.2/1.0 (d)			6.7	6.7	6.7			
Home	0.4/0.5 (m)	13.3(b)		13.3	13.7	12.4	13.7	20.4	13.7
Commuting (in-transit)	1.1/2.4 (m)	1.0(a)	1.0(a)	1.0(f)	1.0(f)	1.0(f)	1(a)	1(a)	7.7
Urban (Outdoors)	0.2/0.39	2.6(a)	2.6(a)	2.6	2.6	2.6	7.6 <sup>g</sup>	2.6	2.6
Home with smokers	0.5/1.0 (c)		13.7(b)			1.3(e)			
Shopping Mall/Market	1.0/1.8 (m)	0.4(i)		0.4(i)					
Bar or Bingo Hall	10.5/25.6 (k)								
INTEGRATED EXPOSURE (ug-hrs/m <sup>3</sup> )		8.7/17.5	9.8/23.8	8.7/17.5	8.4/17.0	8.6/17.6	8.4/13.9	9.8/13.6	14.5/26.3

TIME WEIGHTED AVERAGE EXPOSURE ( $\mu\text{g}/\text{m}^3$ over 24 hr) (h)	0.4/0.7	0.4/1.0	0.4/0.7	0.4/0.7	0.4/0.7	0.4/0.7	0.4/0.7	0.4/0.6	0.4/0.6	0.6/1.1
INTAKE/DAY ( $\mu\text{G}/\text{DAY}$ ) (h)	7.2/14.6	8.2/19.8	5.1/ 10.2	1.8/3.7	7.0/11.6	8.2/11.3	12.1/22.0			

Estimations:

- \* INTEGRATED EXPOSURE (ug-hrs/m<sup>3</sup>) = SUM OF[Microenvironment concentration x Time spent in Microenvironment]
- \* TIME WEIGHTED AVERAGE EXPOSURE (ug/m<sup>3</sup>) = INTEGRATED EXPOSURE/24 hr
- \* INTAKE/DAY (ug/day) = TIME WEIGHTED AVERAGE EXPOSURE x DAILY BREATHING RATE (ie. for Adult or Youth or Child as applicable)

Footnotes:

- a.) TIME BUDGET ANALYSIS; Windsor '91 Summer PEP Study; Handout to Volunteers; May/92 (R. Bell)
- b.) Sum of 'Indoor, Home' and 'Indoor Other' in a.)
- c.) This value was obtained during the personal exposure study in Windsor from homes where smoking was permitted.
- d.) Assumed to be same 'microenvironment' concentration that were measured by PEP study in the 'Office' environment.
- e.) Average time spent in proximity to tobacco smoke, in various locations outside the home, was approximately 1.3 hours, based on a study of children's activity patterns; (Ref: Study of Children's Activity Patterns, State of California, Air Resources Board, Contract No. A 733-149). Assume that benzene concentrations, when in proximity to tobacco smoke is represented by the median levels referenced in footnote "c," above.
- f.) Assume 1 hour is spent in the car per day.
- g.) For the 'high-outdoor' receptor, urban outdoor concentrations were assumed to be represented by the 'mean' and 90th percentile concentrations taken from the fixed site monitoring network. Also assume that for this group, the 6.7 hours of 'at work' exposure is divided so that 1.7 hours is spent in the office and 5 hours is added to the 2.6 hours of urban outdoor exposure for a total of 7.6 hours.
- h.) First number is the 'mean'. The second number is the 90th percentile, if available; otherwise it is the maximum value measured.
- i.) Assumed that approximately 2.8 hours per week are spent on malls shopping; this was distributed over seven days yielding '0.4 hours/day' in malls.
- j.) Assumed that this receptor spends approximately 7 hours per week in a bingo hall or bar; this was distributed over seven days yielding '1 hr/day' in bingo halls or bars.
- k.) 'Bar' and 'bingo hall' data were combined to obtain these values, and these were assumed to be representative of both of these microenvironments.
- l.) Two additional typical personal exposure patterns that were evaluated but are not shown in detail in this table are the 'Average Child in a Smoker Home' and the 'Active Receptor #1' as noted in Table 3 above. The corresponding intakes/day (ie. mean/90th percentile) for these two receptors are 2.0/5.0 and 15.5/35.1, respectively.
- m.) The 'mean' and '90th percentile' concentrations for the 'Office', 'Home' and 'Commuting' microenvironments were derived from the Summer 1991 and Winter 1992 personal exposure studies in Windsor (Note: For 13 - butadiene, data was available only from the Winter 1992 study). For the 'office' microenvironment, the two values represent the minimum and maximum values, since there were insufficient detectable values to calculate a mean.
- n.) These two values represent the minimum and maximum values in a limited data set.



A microenvironment, in which measurements were not taken, but which may be a source of 1,3-butadiene exposure, common to all the above receptors, is the bathroom during bathing and showering.

Volatile organic chemicals will partition from the hot water during showering and bathing and be inhaled by the person in the bathroom. As is noted below in s. 3.2.4.1, no measurements of the concentration of 1,3 butadiene are available. Because of its high vapour pressure (2100 mm Hg at 25°C) and because it is a gas at normal temperature and pressure (boiling point at 1 atm is -4.4°C), it partitions preferentially to air. Its concentration in water is likely to be very low and hence the amount released during showering (which cannot at present be quantified) would be considered insignificant.

In order to place the above inhalation exposures (ie. intakes) in Windsor, in perspective, it is appropriate to compare to daily intakes that people who smoke may experience.

### 3.1.3 Smoking.

1,3-butadiene has been detected in cigarette smoke and exposure occurs both through direct inhalation by smokers and from side-stream smoke. The average total amount in sidestream smoke is 205-361 ug/cigarette with an average airborne yield of 400 ug/cigarette. Indoor air in locations such as bars and taverns where cigarette smoking is common has considerably higher concentrations of 1,3-butadiene than the outdoors<sup>1</sup>. Brunneman *et al.*<sup>19</sup> found 300-470 ug/cigarette in sidestream smoke and 16-75 (ie. an average of = 46 ug/cigarette) in mainstream smoke.

A person who smokes a pack a day (25 cigarettes) would therefore inhale about 1150 ug 1,3-butadiene (46 ug/cigarette). The lower and upper bounds would be 400 and 1875 ug. On the average, the average intake is about 40 times the personal exposures (ie. Table 5). U.S EPA (IRIS<sup>2</sup>) suggests a 20% absorption rate at low exposure levels.

Non-smokers who are heavily exposed to environmental tobacco smoke inhale the equivalent of 1/3 to 3 cigarettes<sup>20</sup> per day or 5 to 225 ug/day using the upper and lower bounds. Vainio<sup>21</sup> states that the exposure of non-smokers to environmental tobacco smoke would be about 1% of that of active smokers or 4 to 20 ug/day, whereas Remmer<sup>22</sup> gives an upper limit of the equivalent of only 1/5 of a cigarette per day or about 3 to 15 ug/day. Hiller<sup>23</sup>, quoting other authors, gives intakes ranging from a low of 0.001 cigarette equivalents (CE)/hr or 0.01 CE/day, assuming 12 hr exposure, to a high of 27 CE/day. The higher value is clearly anomalous as the range claimed by the other authors is 0.001 to 0.2 CE/hr. The lower value gives an intake of 0.2 to 0.8 ug/day.

It is also important to place the inhalation exposures (ie. intakes) in Windsor into perspective, relative to general exposures from other media (ie. see section 3.2).

## 3.2 Other Routes

In this section, possible non-inhalation routes of exposure (ie. ingestion and dermal) are estimated.

### 3.2.1 Ingestion of Food

1,3-butadiene is used to manufacture synthetic rubber and plastics for food packaging. Measurements of the packages and the contained foods have shown high residues in the packages (20 ng/g to 310 ug/g), but only in few instances (olive oil at =8 ng/g) have any residues been found in the food. Therefore, the migration from the packaging to foods is unlikely to present a problem and the intake from food is likely to be insignificant<sup>1</sup>.

### 3.2.2 Drinking Water

The Ministry's drinking water testing program has not analysed for 1,3-butadiene. The chemical has been qualitatively identified in US drinking water and has been identified in only 1 of 204 samples of surface waters close to known industrial sources. The concentration was 2 ug/L<sup>1</sup>. Because of its high vapour pressure (2100 mm Hg at 25°C) and because it is a gas at normal temperatures (boiling point at 1 atm is -4.4°C<sup>1</sup>), it partitions preferentially to air. Therefore, its concentration in water is likely to be low and the intake from drinking water, which cannot at present be quantified, is likely to be insignificant.

### 3.2.3 Soil

Volatile compounds, including 1,3-butadiene, were not measured in soils in the Windsor Air Quality Study. No data was found in the available literature<sup>1</sup>. Because of its physical and chemical properties, it is not expected to adsorb significantly to soil. Therefore, its concentration in soil is likely to be low and the intake from soil, which cannot at present be quantified, is likely to be insignificant.

### 3.2.4 Dermal

#### 3.2.4.1 During Showering and Bathing

Because the concentrations in water are not known, this pathway cannot be quantified. However, as the concentration of 1,3-butadiene in water is believed to be low, this pathway is likely to be insignificant.

#### 3.2.4.2 Contact With Soil and Dirt

Because the concentrations in soil are not known, this pathway cannot be quantified. However, as the concentration of 1,3-butadiene in soil is believed to be low, this pathway is likely to be insignificant.

#### 3.2.4.3 From 1,3 - Butadiene Vapour in the Air

The absorption through the skin of vapors in the air can be calculated from the formula

$$DA_{\text{event}} = K_p^{\text{air}} C_{\text{air}} t_{\text{event}}$$

where

$DA_{\text{event}}$  is the absorbed dose per event (mg/cm<sup>2</sup>-event)

$K_p^{\text{air}}$  is the permeability constant (cm/hr)

$C_{\text{air}}$  is the concentration of the vapor in air (mg/cm<sup>3</sup>)

$t_{\text{event}}$  is the exposure time (hr/event)

There are no values for the permeability constant for 1,3-butadiene (ie. in table 7-1 or table 7-7 in US-EPA<sup>13</sup>) and most of the available values are for chlorinated compounds. The values for aliphatics range from ≈ 0.04 cm/hr to ≈ 0.2. The  $K_p$  for isoprene is < 0.01 cm/hr. Since isoprene differs from 1,3-butadiene by one methyl group it is reasonable to assume that the permeability constant for 1,3-butadiene is close to that of isoprene.

From the scenarios in Table 4, a reasonable range in time weighted air concentrations is 0.4 to 2 ug/m<sup>3</sup> or 0.4 - 5 × 10<sup>-9</sup> mg/cm<sup>3</sup>. The median surface area for an adult is 1.94 m<sup>2</sup> and for a child, 0.73. The

exposure time is 24 hrs.

Using the range of air concentrations and a permeability coefficient of 0.01, the doses absorbed per day would be:

adult : 0.002 to 0.01 ug  
child: 0.0007 to 0.004 ug

#### 4. RISK CHARACTERIZATION AND PERSPECTIVES

Exposures, expressed as daily intakes in units of ug/day, were assessed in section 3. Inhalation, ingestion and dermal routes of exposure were considered. Table 5 below summarizes the daily intakes (or ranges of daily intakes) of 1,3 - butadiene, for adults and children, estimated in section 3. It should be noted that in section 3, the intakes for inhalation and sometimes for ingestion assumed 100% bioavailability. The intake for dermal exposures are amounts absorbed systemically and hence already include bioavailability considerations. Table 5 has two columns for both adults and children. The first set of columns (ie. '100 % Bioav') give the intakes with 100 % bioavailability having been assumed; the second set (ie. "Bioav. Incl."), gives intakes for which bioavailability has been taken into consideration (ie. if information was available as noted in the footnotes). This second set of columns should give a better picture of the relative importance of various exposure routes. As far as comparison to exposure guidelines and intakes associated with cancer risk, the intakes in the first set of columns of Table 5 will be used since the exposure guidelines are also expressed as intakes for which we have assumed 100 % bioavailability.

To characterize risks, the various exposure guidelines discussed in Section 2 are compared to the estimated exposures from inhalation and other routes as discussed in Section 3. Because of the assumptions, uncertainties and ranges of values available from both exposures (see Table 5) and the various exposure guidelines (see Table 1), risk characterization is most appropriately done by comparison of ranges of values.

Table 6 below provides a graphic representation of this comparison of exposures, exposure guidelines and intakes associated with inhalation cancer risk, based on ug intake/day (ie. 'INTAKE in Micrograms per day' increasing upwards on the vertical scale).

The middle section of Table 6, "Exposures", depicts the exposures calculated in Section 3, expressed as intake/day (ie. ug/day). The exposures depicted are: *Outdoor Air Quality* - the exposure from spending 100 % of the day outdoors; *Typical Outdoor Exposure* - the exposure from three hours only outdoors, provided for perspective on the contribution to risk solely from contaminants present in outdoor air; *Typical Personal Exposures* - the range of exposures associated with ten different exposure scenarios, combining periods of indoor, outdoor and various microenvironment exposures. Exposure scenarios are included for adults and children, assuming 20 and 5 m<sup>3</sup>/day inhalation rates respectively. For 'outdoor air quality' (ie. 100% outdoor exposure), for 'typical outdoor exposures' (ie. 3 hr), and for the 'typical activity patterns' the ranges shown, bracket the lowest mean to the highest 90th percentile. For perspective purposes, the exposures of smokers, directly from smoking activity is also depicted in this section.

The left section of Table 6, "Exposure Guidelines", expresses the various guidelines discussed in Section 2 in terms of calculated "allowable" intake/day for adults and children. The values are taken from Table 1. Within each type of guideline group (eg. outdoor air) ranges of exposure guidelines, when available, are indicated. Thus, ranges of Air Quality Guidelines (ie. 'Outdoor Air'), Occupational guidelines (ie.



'Workplace Air'), and a chronic health effects based reference concentration (ie. 'Chronic AEL'; only one available) are shown. Comparison of "Exposure Guidelines" to "Exposures" should be done with care. For example, occupational guidelines are included for perspective purposes only. For caveats regarding this comparison see section 4.1.1 of the main report.

The right section of Table 6, "Intakes Associated With Cancer Risk", shows the intakes associated with different levels of cancer risk. Ranges of carcinogenic risk levels (associated with  $1 \times 10^{-5}$  risk and  $1 \times 10^{-6}$  risk) are depicted. Comparison of "Exposures" to "Intakes Associated With Cancer Risk" is appropriate for adult exposures only, since cancer risk estimates apply to a lifetime of exposure and people are adults for the majority of their lives. Adult exposures in the bars of the "Exposure" section fall in the top 70 % of the bars which represent exposures of adults and children.

Based on the tabular analysis (Table 5) and the graphic risk characterization (Table 6), the following observations and deductions can be made:

#### Health Messages:

1) It is apparent, that the inhalation route dominates all other exposure routes for 1,3-butadiene. Most exposures by ingestion and via absorption across the skin are thought to be insignificant. Some very limited exposure may occur by dermal exposure from 1,3-butadiene vapour in the air.

2) For a non smoker, inhalation in various microenvironments and outdoors is the main source of exposure to 1,3-butadiene.

3) All the inhalation exposures associated with outdoor air quality (ie. 100 % outdoor exposure) and with typical outdoor exposure (ie. 3 hr) are less than the chronic threshold effect level (ie. 'Chronic TEL (Mass)' of 24 ug/day in Table 1) proposed by the Massachusetts Department of Environmental Protection (MDEP). However, some of the exposures associated with personal activity patterns slightly exceed this proposed level. This chronic threshold effect level is considered to be purely health based and is protective against all chronic health effects other than cancer risk. Therefore, the possibility of long-term health effects, other than cancer risk, is unlikely with all inhalation exposures, except for some exposures associated with personal activity patterns. These personal exposure areas appear to include the tobacco-smoke affected environments.

This comparison of exposures to chronic acceptable exposure levels can also be expressed more quantitatively in the form of a hazard index. These hazard index comparisons for all substances are summarized and are found in section 4.1.5 of the main report.

4) The most stringent and conservative range of available exposure guidelines are depicted in Table 6 under Intakes Associated with Cancer Risk. These guidelines were proposed by CDHS, the US EPA, and the U.S. Occupational Safety and Health Administration (OSHA). As shown in Table 6, they overlap with and are exceeded by the estimated exposures. Because people are adults for the majority of their lives, these intakes associated with cancer risk are depicted for adults only. The inhalation intakes for adults associated with 'outdoor air quality' (ie. 100 % outdoor exposure), 'typical outdoor exposure' (ie. 3 hr) and 'typical personal exposures' range between 4 - 7.8 ug/day, 0.5 - 1 ug/day and 7 - 35 ug/day, respectively (from Tables 2, 4 and 5). These intakes and the corresponding doses in mg/kg-day are summarized in Table 7. Using the various potencies from the three agencies, the range of risks associated with 'outdoor air quality' (ie. 100% outdoor exposure) is between  $1.5 \times 10^{-6}$  and  $1.1 \times 10^{-4}$ . Similarly the range of risks associated with 'typical outdoor exposures' (ie. 3 hr) is between  $1.9 \times 10^{-7}$  and  $1.4 \times 10^{-5}$ . Similarly the range of risks associated with 'typical personal exposures' is between  $2.7 \times 10^{-6}$  and  $5.0 \times 10^{-4}$ . The risks associated with 'typical personal exposures' are slightly higher than the risks associated with 'outdoor air quality' which in turn is higher than 'typical outdoor exposures'. This range of risk analysis



Table 5. Summary of Estimated Daily Intakes and/or Range of Intakes (in ug /day), from Various Exposure Pathways (ie. intakes, assuming 100 % bioavailability and intakes with bioavailability taken into consideration)

EXPOSURE PATHWAY		ADULT ug/day  (100 % Bioav.)	ADULT ug/day  (Bioav. Incl.)	CHILD ug/day  (100 % Bioav.)	CHILD ug/day  (Bioav. Incl.)
INHALATION	Outdoor Air Quality - Windsor (ie. 100 % outdoor exposure)(a)	4.0 - 7.8	0.8 - 1.6 (f)	1.0 - 2.0	0.2 - 0.4 (f)
	Typical outdoor exposure (ie. = 3hr)(b)	0.5 - 1.0	0.1 - 0.2 (f)	0.13 - 0.25	0.03 - 0.05 (f)
	Typical personal exposures(ie. Table 4) (c)	7.0 - 35.1	1.4 - 7.0 (f)	1.8 - 5.0	0.4 - 1.0 (f)
	Smoking (e)	400 - 1900	80 - 380 (f)		
INGESTION	Food	d		d	
	Drinking water	d		d	
	Soil	d		d	
	TOTAL (Ingestion)				
DERMAL	During showering		d		d
	Contact with soil & dirt		d		d
	From 1,3-butadiene vapour in the air		0.002 - 0.01		0.0007 - 0.004
	TOTAL (Dermal)		0.002 - 0.01		0.0007 - 0.004

a.) Range of intakes is associated with the range of the 'mean' to '90th percentile' concentrations in outdoor air. It is to be noted that people are not exposed 24 hours to outdoor air. This estimation assumes 100 % exposure to outdoor air and is a measure of outdoor air quality per se and not of actual exposure.

b.) Range of intakes calculated from the 'mean' to '90th percentile' concentrations in outdoor air and assuming a 'typical' outdoor air exposure of = 3 hr(ie. corresponding to breathing 2.5 m<sup>3</sup>/3hr for adults and 0.63 m<sup>3</sup>/3hr for children.

c.) Range of intakes is estimated from the range of the lowest 'mean' and the highest '90th percentile' concentrations obtained from personal exposure and microenvironment measurements.

d.) Believed to be insignificant because of the chemical and physical properties of 1,3 - butadiene. Quantification is not possible because of lack of data.

e.) The intake shown is the direct intake (ie. from lower to upper bound estimate) of an adult smoker from smoking activity (ie. 'smoking') only. Various smoking environments for adults and children have already been included in the 'typical personal exposure' scenarios.

f.) The absorption rate is 20% (see s. 1.1 and s. 3.1.3).

is summarized in Table 7. It should be further noted, that this risk characterization (ie. using carcinogenic

Table 6. 1,3-BUTADIENE RISK CHARACTERIZATION in WINDSOR  
 Ranges of exposure guidelines, exposures and risk estimates  
 (Inhalation unless otherwise specified)



risk based limits) is based on an assumed lifetime exposure (i.e., 24 hours, every day, for 70 years) and hence is a very conservative assumption.

5) The exposure that a smoker experiences is considerably higher than any of the exposures associated with 'personal activity patterns', 'outdoor air quality' and 'typical outdoor exposures'.

6) For a smoker, the inhalation exposure is dominated by the 1,3-butadiene in cigarettes. Adding an additional exposure of 30 ug/day from air to the 1150 ug/day (ie. average) from cigarettes leads to an average total intake of 1180 ug/day. As noted previously, the maximum intake could be as high as 1875 ug/day (1905 ug/day, when adding 30 ug/day from air). The average to high intakes correspond to doses of 0.017 to 0.027 mg/kg-day. The corresponding risks for the average intake are  $1.7 \times 10^{-3}$  (EPA) or  $1.0 \times 10^{-2}$  (CDHS) and for the high intake  $2.7 \times 10^{-3}$  (EPA) or  $1.6 \times 10^{-2}$  (CDHS).

**Table 7. Range of Inhalation Cancer Risks Associated with Estimated Intakes (ie. for adult exposures only) of 1,3 - Butadiene**

RANGE of INHALATION INTAKES			POTENCY (a)		RANGE of RISKS
Environment	Unit ug/day	Unit mg/kg/day	Agency	Unit (mg/kg-d) <sup>1</sup>	
OUTDOOR AIR QUALITY (Windsor)	4 - 7.8	$5.7 \times 10^{-5}$ - $1.1 \times 10^{-4}$	EPA	1.0	$5.7 \times 10^{-5}$ - $1.1 \times 10^{-4}$
			CDHS	$6.1 \times 10^{-1}$	$3.5 \times 10^{-5}$ - $6.7 \times 10^{-5}$
			OSHA	$2.7 \times 10^{-2}$	$1.5 \times 10^{-4}$ - $3.0 \times 10^{-4}$
			OVERALL RANGE OF RISKS: $1.5 \times 10^{-4}$ - $1.1 \times 10^{-4}$		
TYPICAL OUTDOOR EXPOSURE (ie.≈ 3 hr.)	0.5 - 1	$7.1 \times 10^{-6}$ - $1.4 \times 10^{-5}$	EPA	1.0	$7.1 \times 10^{-6}$ - $1.4 \times 10^{-5}$
			CDHS	$6.1 \times 10^{-1}$	$4.3 \times 10^{-6}$ - $8.5 \times 10^{-6}$
			OSHA	$2.7 \times 10^{-2}$	$1.9 \times 10^{-7}$ - $3.8 \times 10^{-7}$
			OVERALL RANGE OF RISKS: $1.9 \times 10^{-7}$ - $1.4 \times 10^{-5}$		
TYPICAL PERSONAL EXPOSURES	7 - 35	$1.0 \times 10^{-4}$ - $5.0 \times 10^{-4}$	EPA	1.0	$1.0 \times 10^{-4}$ - $5.0 \times 10^{-4}$
			CDHS	$6.1 \times 10^{-1}$	$6.1 \times 10^{-5}$ - $3.1 \times 10^{-4}$
			OSHA	$2.7 \times 10^{-2}$	$2.7 \times 10^{-4}$ - $1.4 \times 10^{-3}$
			OVERALL RANGE OF RISKS: $2.7 \times 10^{-4}$ - $5.0 \times 10^{-4}$		
a. These are equivalent potency factors calculated from the unit risks proposed by the agencies listed; assumed adult weight of 70 kg and 20 m <sup>3</sup> per day.					

7) Considering the information in Table 5 the exposures from the *non-inhalation* pathways are:

- *Ingestion* of food, water and soil:  
Intake considered to be insignificant
- *Dermal* absorption:

From 1,3-butadiene vapour in the air: adult - 0.002 to 0.01 ug/day

child - 0.0007 to 0.004 ug/d

These dermal exposures are 50 to over 1000 times less than from inhalation. Dermal exposure could still be significant in view of the lipophilic nature of 1,3-butadiene. Therefore, in some cases, dermal exposure may add to the cancer risks from exposure to 1,3-butadiene.

#### Regulatory compliance messages:

8) The risk characterization in Table 6 indicates that, for the inhalation receptor exposures considered:

- The exposures potentially associated with outdoor air quality, for adults, youth and children, exceed the air quality guidelines of various jurisdictions.
- Exposures associated with typical outdoor exposure (ie. 3 hr) overlap with the air quality guidelines of various jurisdictions
- Exposures associated with personal activity patterns also exceed the air quality guidelines of various jurisdictions.

It should be noted that these air quality guidelines may be of different types. Some are purely health based and some are regulatory and therefore may have been influenced by various risk management considerations. The regulatory guidelines may also have different uses (eg. judging the acceptability of air quality per se or judging the incremental addition by a source to the existing air quality).

9) Table 6 also indicates that all the inhalation exposures are less than the range of occupational guidelines (Table 6 indicates that intakes associated with occupational guidelines extend 'up to 44,000,000' ug/day).

10) MOEE is presently reviewing 1,3-butadiene for the purpose of standard setting.

#### Summary and recommendations:

- ♦ All the inhalation exposures, except some personal exposures associated with tobacco smoke-affected environments, are less than the chronic threshold effect level. Therefore, the possibility of long-term health effects, other than cancer risk, is unlikely with all inhalation exposures, and possible for some exposures associated with personal activity patterns.
- ♦ The range of estimated inhalation risks associated with 'outdoor air quality' (ie. 100% outdoor exposure) is between  $1.5 \times 10^{-6}$  and  $1.1 \times 10^{-4}$ . Similarly, the range of risks associated with 'typical personal exposures' is between  $2.7 \times 10^{-6}$  and  $5.0 \times 10^{-4}$ . Since these levels of risk exceed  $1 \times 10^{-5}$ , a level generally deemed to be negligible, it is recommended that 1,3-butadiene be considered a candidate for reduction of exposure.
- ♦ Exposure and therefore risks associated with 'typical personal exposures' are slightly higher than the risks associated with 'outdoor air quality'.
- ♦ The commuting and tobacco smoke-affected environments are the most dominant in the upper range of 'typical personal exposures'.
- ♦ The exposure that a smoker experiences is considerable higher (ie. associated risks are between 1.7

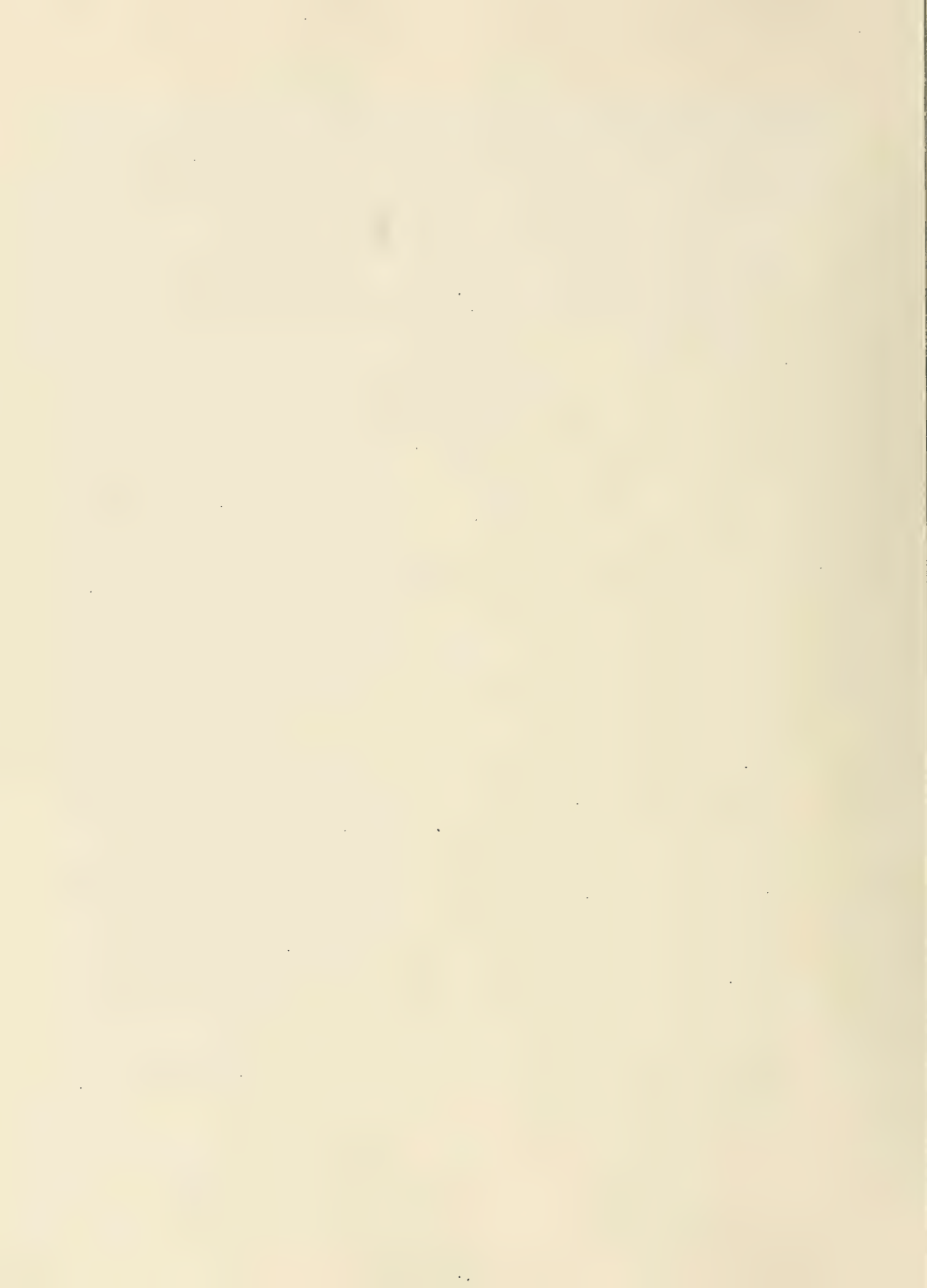


$\times 10^{-3}$  and  $1.6 \times 10^{-2}$ ) than the exposures associated with 'personal activity patterns' and 'outdoor air quality'.

♦ Exposures from ingestion are considered to be insignificant and dermal exposures are 50 to 1000 times less than from inhalation.

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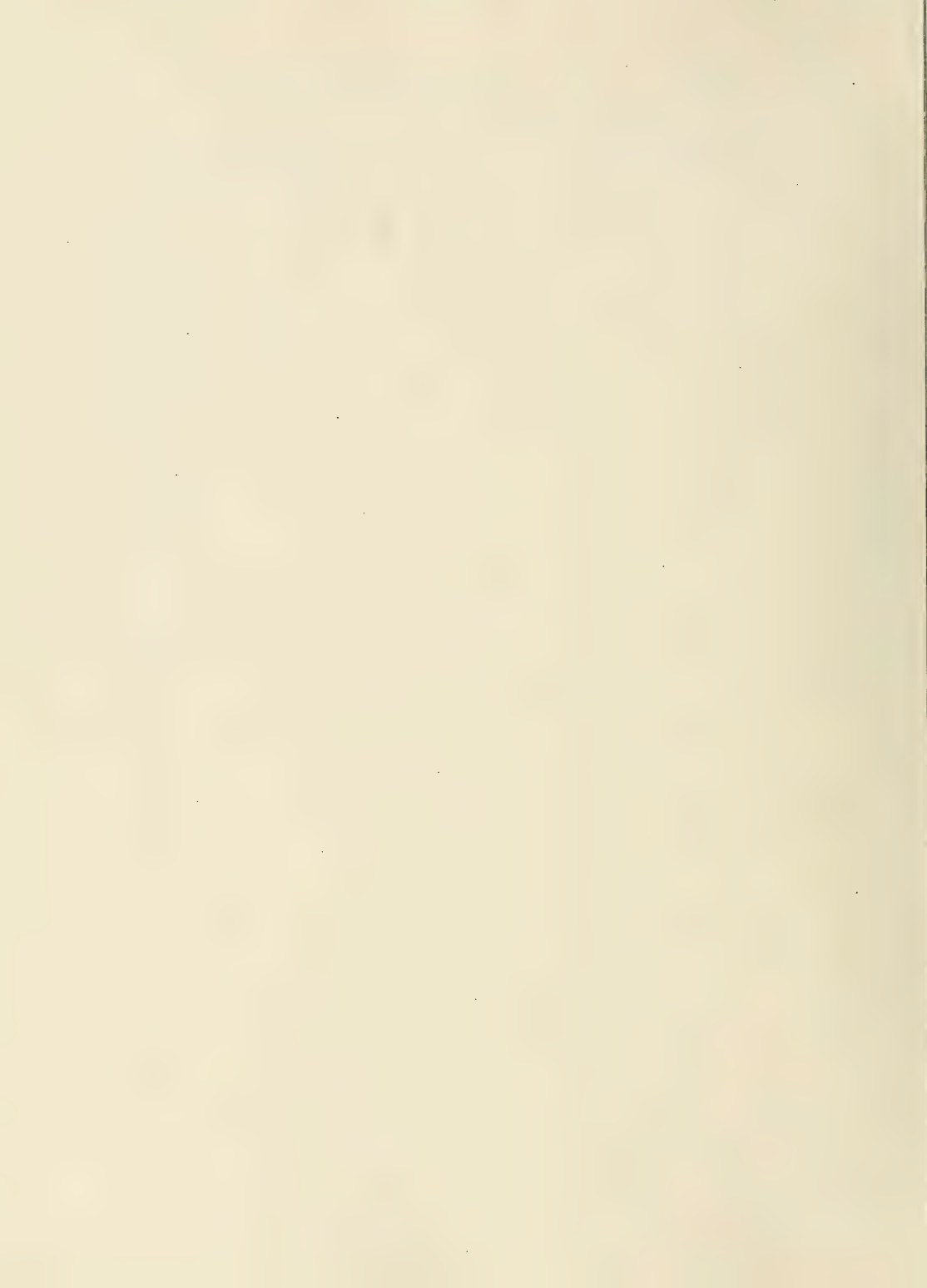
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### **APPENDIX 3**

### **RISK ANALYSIS FOR CARBON TETRACHLORIDE**





## APPENDIX 3

### RISK ANALYSIS FOR CARBON TETRACHLORIDE

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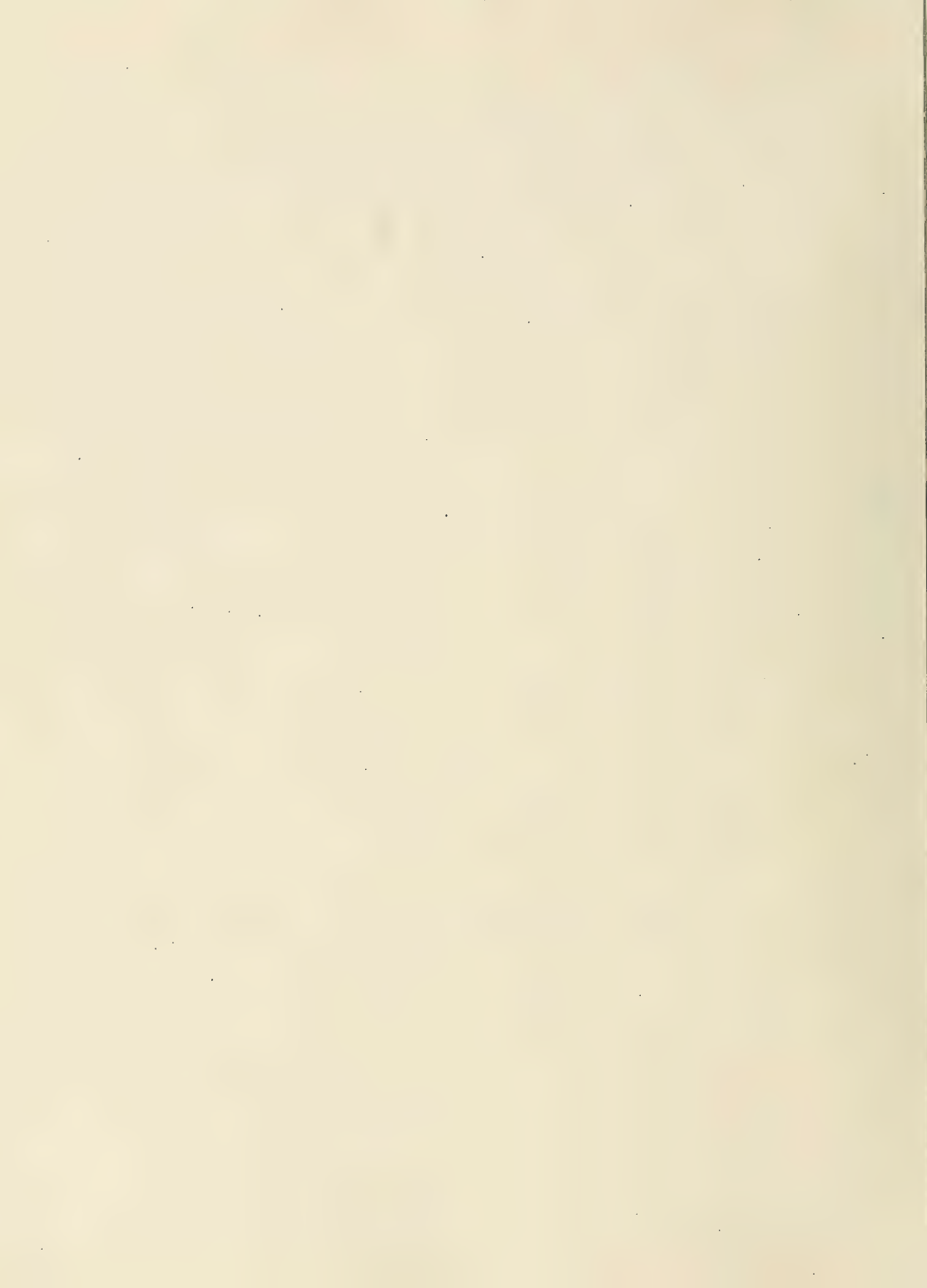
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## CARBON TETRACHLORIDE

### DESCRIPTION and SOURCES of CARBON TETRACHLORIDE.

Carbon tetrachloride ( $\text{CCl}_4$ ) is a liquid with a sweet odour. It evaporates easily and therefore it is often found in the environment in gaseous form. Most of the carbon tetrachloride that is emitted to the environment is found as a gas in the atmosphere. Because of its persistence, it can remain in the air for several years.

Carbon tetrachloride does not occur naturally. The major current use of carbon tetrachloride is in the production of chlorofluorocarbons (CFCs) which are used primarily as refrigerants and as propellants for aerosol cans. Since CFCs have been found to affect the earth's ozone layer, the production of these chemicals is being phased out. Previously, carbon tetrachloride was widely used as a cleaning/degreasing agent in the dry cleaning industry and in the home it was used as a spot remover from carpets and clothes. In 1990, an estimated total of 1,671,000 pounds of carbon tetrachloride was discharged to the air from manufacturing and processing facilities in the U.S.

### 1. ° HAZARD IDENTIFICATION

An extensive review on the toxicology, human epidemiology, environmental fate, and properties of carbon tetrachloride was published recently by the Agency for Toxic Substance and Disease Registry (ATSDR) of the US Department of Health and Human Services, Public Health Service<sup>1</sup>. The review, which encompasses past and recent findings obtained from a detailed literature search, provides an excellent integrative and interpretative evaluation of the carbon tetrachloride issue as related to its potential health effects on humans following exposure through various environmental pathways. As it is the scope of the current document to provide a general, although comprehensive updated overview on the toxicology of carbon tetrachloride, excerpts of the recent ATSDR document were used in the following sections to summarize the information considered to be of relevance for the Windsor study. A more detailed discussion of the health effects of carbon tetrachloride may be obtained by consulting references contained in section 5<sup>1,2,4</sup>.

#### 1.1 Absorption and Metabolism

In view of the ubiquity of carbon tetrachloride in the various environmental compartments, exposure may occur through various routes. These include inhalation of vapours and/or contaminated air, ingestion of contaminated food and water, and dermal uptake. The first two are considered to be significant for the general population, while dermal uptake may be of considerable importance for workers exposed to substantially higher concentrations in occupational settings. In the latter case, however, the method of application will determine the bioavailability of the compound, with vapor uptake being relatively minimal when compared to absorption following dermal contact with liquid carbon tetrachloride. Results for the pulmonary bioavailability in humans are scanty, and therefore animal-based data are frequently used for such purposes. Early reports suggest that bioavailability in humans might be as high as 60%, while monkeys have been found to absorb an average of 30% of the total amount of carbon tetrachloride inhaled. In their risk assessment for carbon tetrachloride, the US EPA<sup>5</sup> retained a value of 40%, based on 30% inhalation in monkeys, and 30% and 57-65% inhalation in humans. Results for oral exposure based on animal studies are more consistent, with the average bioavailability attaining 80% depending on the vehicle (e.g., corn oil decreases absorption) and exposure conditions. Overall, the bioavailability of carbon tetrachloride by all three routes of exposure is considered significant.

Following systemic absorption, carbon tetrachloride is rapidly distributed to all major organs and tissues, with highest concentrations in the fat, bone marrow, brain and spinal cord, liver, blood, kidney, and



muscles. The metabolism of carbon tetrachloride, considered a bioactivation step, is thought to proceed mainly in the liver, and involves cleavage of a C-Cl homolytic bond by cytochrome P-450 enzymes with the subsequent formation of free radicals (e.g.,  $\text{CCl}_3\cdot$ ). These are highly reactive chemical species that readily undergo secondary reactions or bind to cellular macromolecules such as DNA. In the presence of oxygen (aerobic environment), a chain reaction involving oxygenated free radicals, derived from the trichloromethyl radical (e.g.,  $\text{CCl}_3\text{OO}\cdot$ ), and membrane lipid may take place resulting in the oxidative destruction of cellular and intracellular membranes, loss of cellular function, and eventually cell death. This reaction, better known as lipid peroxidation or LPO, is thought to be the molecular mechanism by which carbon tetrachloride induces its toxic effects<sup>3</sup>. Secondary products of carbon tetrachloride metabolism that have been measured include chloroform ( $\text{CHCl}_3$ ), carbon monoxide, and phosgene ( $\text{Cl}_2\text{CO}$ ).

Excretion of inhaled carbon tetrachloride in humans is rapid, and occurs according to a biexponential model with a half-life for the rapid phase of less than 1 hour. More detailed pharmacokinetic studies conducted in animal have indicated that 30-40% of the inhaled carbon tetrachloride is eliminated through the pulmonary route as the parent chemical, with only small amounts as carbon dioxide. 50-60% seems to be eliminated through the feces, although the identity of these metabolites has not been identified. The half-life for the rapid phase observed in animals is in the order of 7-10 hours. Comparable observations were noted for the ingestion route, with a higher fraction of carbon tetrachloride being exhaled unchanged at high doses of exposure.

## 1.2 Toxicology

Several fatal cases of human poisoning have been reported following exposure to high concentrations of carbon tetrachloride. These cases were characterized by hemorrhagic congestion and lung edema, secondary to severe renal injury. However, the concentrations at which these effects occurred (630-3150  $\text{mg}/\text{m}^3$ ; 100-500 ppm) are of little relevance to the general population with the exception of accidental releases, spills, and poisoning cases.

Carbon tetrachloride is a recognized multifaceted toxicant that induces adverse effects in various organs and tissues. Several case studies in humans have documented effects to the respiratory, cardiovascular, gastrointestinal, neurological, and hematological system. The liver and kidney appear to be the most sensitive organs to the effects of carbon tetrachloride. Generally, these effects have been observed in animals for which, contrary to humans, there is also evidence of reproductive and developmental disturbances. It has been demonstrated, however, that these effects occur at relatively high exposure concentrations/doses which are not expected to be encountered in the general environment.

Chronic daily intake of low levels of carbon tetrachloride by both the inhalation and oral routes is considered the most relevant exposure scenario for human populations, although little information is available to properly address this issue. As a result, data obtained from animals studies are generally used as surrogate models of long-term toxicity. The effects associated with long-term inhalation of carbon tetrachloride vapors have included the development of mild hematological effects (100 ppm for 10 months), mild to moderate liver effects (10-50 ppm for several months or more), kidney nephropathies (50 ppm for 9 months), neurological disturbances (50 ppm for several months), and reproductive/developmental effects (200-250 ppm) (Figure 1.1). A No Observed Adverse Effect Level (NOAEL) for liver effects in animals has been established at 5 ppm. ATSDR also reports that no studies were located regarding carcinogenicity in animals after inhalation exposure to carbon tetrachloride. On the other hand, occasional reports have noted the occurrence of liver cancer in humans who had been exposed to carbon tetrachloride fumes, both acutely and for longer periods. It appears however that the evidence is much too sparse to establish a cause-effect relationship.

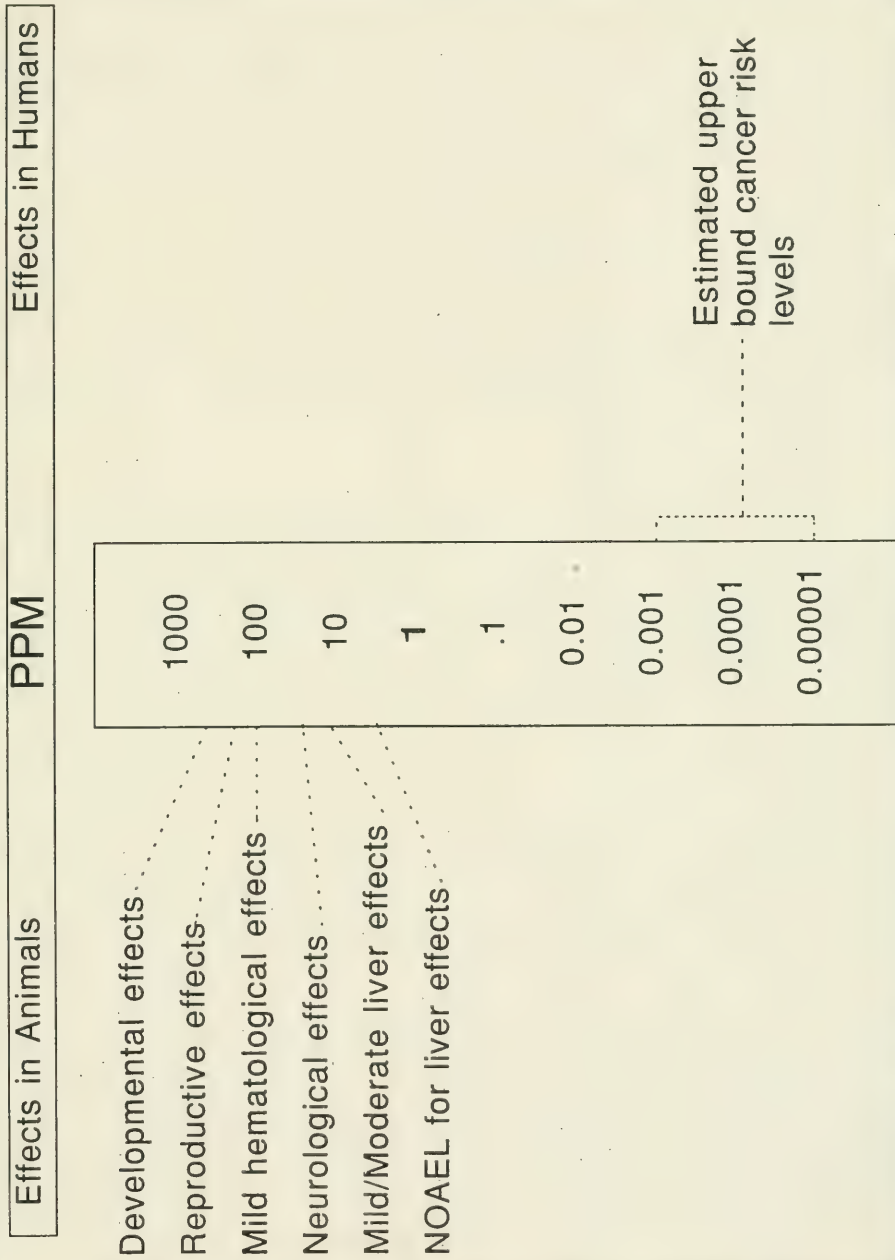


Figure 1.1 Summary of chronic effects associated with the inhalation of various concentrations of carbon tetrachloride (adapted from 1)(1ppm corresponds to 6.3 mg/m<sup>3</sup>)

# Effects in Humans

## mg/kg-day

## Effects in Animals

LOAEL for kidney effects  
(90 days)

Liver cancer  
NOAEL for liver effects  
(2 year)

Reproductive effects

1000

100

10

1

.1

0.01

0.001

0.0001

0.00001

Estimated upper  
bound cancer risk  
levels, in ug/kg-day

Figure 1.2 Summary of chronic effects associated with oral exposure to various doses of carbon tetrachloride (adapted from 1)

Information regarding the effects induced by chronic oral exposure in humans is absent, and that available from animals is incomplete (Figure 1.2). This situation may be explained by the fact that investigators have concentrated their attention to neoplastic effects known to be induced by exposure to carbon tetrachloride, and to neglect other effects which may occur at comparable doses of exposure. Indeed, studies in animals (rats, hamsters, and several strains of mice) have provided convincing evidence that ingestion of carbon tetrachloride increases the risk of liver cancer. In general, liver tumors (hepatomas or hepatocellular carcinomas) appeared after exposure periods of only 10-30 weeks to daily oral doses as low as 20 mg/kg. In these cases the incidence of hepatic tumors reached 75-100%<sup>5</sup>.

Based on these animal studies, the carcinogenicity of carbon tetrachloride has been recognized by various regulatory agencies and organizations. The International Agency for Research on Cancer (IARC) has classified carbon tetrachloride in group 2B, *i.e.*, possibly carcinogenic to humans, based on inadequate evidence in humans but sufficient evidence in animals<sup>6</sup>. The US Environmental Protection Agency, on the other hand, considers carbon tetrachloride as a probable human carcinogen (Class B2). It is interesting to note that despite the carcinogenic effect displayed by this chemical, no evidence of genotoxic activity has been detected so far in a battery of *in vitro* and *in vivo* bioassays<sup>1</sup>, including human peripheral lymphocytes. This suggests the involvement of epigenetic mechanisms of carcinogenesis, an hypothesis which is in accord with the observations that liver tumors appear mostly in animals that have suffered significant hepatic damage and have undergone extensive hepatic regeneration.

## 2. DOSE-RESPONSE INFORMATION/CURRENT EXPOSURE GUIDELINES

The uncertainties surrounding the potential toxicological effects of environmental carbon tetrachloride on communities have influenced the methodologies used to set guidelines and permissible exposure levels. As noted previously, the adoption of reasonably conservative assumptions is warranted in this context in order to provide sufficient protection of public health. This section summarizes various health criteria values, that is, exposure guidelines and dose-response information that leading regulatory agencies (and other relevant sources) have proposed and consider appropriate for permitting, assessing, and characterizing risks associated with various exposures. Potential exposures to carbon tetrachloride are evaluated in section 3 and the risk characterization is presented in section 4.

### 2.1 Air Guidelines

#### 2.1.1 Chronic, Non-Carcinogenic Health Effects

The US EPA's Integrated Risk Information System database<sup>8</sup> notes that the inhalation Reference Concentration (RfC) for carbon tetrachloride is not available at this time. EPA defines an RfC as an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. The equivalent notation for the oral route is the Reference Dose (RfD), and the value proposed by the US EPA is of 0.7 ug/kg-day. This value was derived from a NOAEL based on liver effects in rats.

The California Department of Health Services<sup>7</sup> has reported for carbon tetrachloride, in January 1992, an inhalation chronic AEL (Acceptable Exposure Level) of 2.4 ug/m<sup>3</sup>. These values have the same purpose as the US EPA's RfC, *i.e.*, they are used for the evaluation of the potential noncancer adverse health effects of long-term (chronic) exposures. In this particular case, the California AEL was derived based on the US EPA's RfD by assuming a 70 kg person breathes 20 m<sup>3</sup> per day and equal absorption occurs by the inhalation and oral routes. Based on the information reported in Section 1.1 on the bioavailability of carbon tetrachloride, this assumption is considered conservative. The validity of this approach, therefore, is conditional to the induction of similar qualitative and quantitative adverse effects by both routes of



exposure, an aspect which has not been completely resolved yet for carbon tetrachloride.

The Massachusetts Department of Environmental Protection<sup>8</sup> has proposed in 1990 a Threshold Effects Exposure Limit (TEL) of 85.5  $\mu\text{g}/\text{m}^3$ , based on the ACGIH occupational exposure guideline. The revision of the ACGIH guideline however is underway, which renders questionable any application of the actual Massachusetts TEL.

Generally, the inhalation chronic AEL, TEL, and the inhalation RfC noted above are comparable in their use for assessing chronic effects (except carcinogenic effects) due to inhalation. It is expected that constraining environmental exposures of human populations to cancer-preventive levels of carbon tetrachloride should decrease to negligible levels, or simply eliminate depending on the end-point of concern, the probability of occurrence of chronic non-cancer health effects.

### 2.1.2 Carcinogenic effects

For the purpose of estimating cancer risk, the U.S. EPA<sup>5</sup> has established an inhalation unit risk of  $1.5 \times 10^{-5} (\mu\text{g}/\text{m}^3)^{-1}$  for continuous lifetime exposure to 1  $\mu\text{g}/\text{m}^3$  of carbon tetrachloride. This value was derived based on a oral potency factor of  $1.3 \times 10^{-1} (\text{mg}/\text{kg}\cdot\text{day})^{-1}$  by assuming an air intake of 20  $\text{m}^3/\text{day}$ , and 40% absorption rate by humans. The oral potency factor, on the other hand, is the geometric mean of 4 different sets of results involving chronic gavage exposure of Syrian Hamsters, mice, and rats.

The California Department of Health Services (CDHS)<sup>7</sup> has established an inhalation unit risk of  $4.2 \times 10^{-5} (\mu\text{g}/\text{m}^3)^{-1}$  associated with lifetime continuous exposure to 1  $\mu\text{g}/\text{m}^3$ . No rationale was provided for the derivation of this value in the above referenced document (ie. Ref.7), although its similarity to the US EPA unit risk factor suggests a common origin as related to the database used. In fact, recalculation of this value suggests that equal absorption was assumed between the oral and pulmonary routes, as compared to the 40% bioavailability value retained by the US EPA. Contrary to the US EPA, however, no oral potency factor was provided by CDHS despite the availability of bioassays results.

The New York State Department of Environmental Conservation (NYSDEC)<sup>9</sup>, the Massachusetts Department of Environmental Protection (MDEP)<sup>8</sup>, and the States of Kansas, Indiana, and Vermont<sup>1</sup> have all used the US EPA unit risk factor to calculate an acceptable ambient air concentrations of 0.07  $\mu\text{g}/\text{m}^3$ , corresponding to an excess lifetime risk of  $10^{-6}$ . This indicates acceptance of the oral potency factor derived by the CAG group of the US EPA and the assumptions regarding bioavailability by the pulmonary route. Higher annual acceptable ambient air concentrations were proposed by the state of North Carolina (6.7  $\mu\text{g}/\text{m}^3$ ) and Texas (13  $\mu\text{g}/\text{m}^3$ ), while a lower annual value of 0.03  $\mu\text{g}/\text{m}^3$  was proposed by the state of Rhode Island<sup>1</sup>.

In their treatise on air toxics and risk assessment, Calabrese and Kenyon<sup>10</sup> reviewed the toxicological evidence for carbon tetrachloride and suggested an Ambient Air Level Goal (AALG) of 0.053  $\mu\text{g}/\text{m}^3$  for an estimated excess lifetime risk of dying from cancer of  $10^{-6}$ . Their approach used the information and unit risk factor proposed by the US EPA, further modified with a Relative Source Contribution (RSC) of 80% to take into account other possible routes of exposure (i.e., 80% of the human exposure was assumed to occur through air, and 20% through ingestion of contaminated water and food).

No cancer potency factors and air guidelines have been proposed by the International Agency for Research on Cancer (IARC) and the World Health Organization, respectively.

The current ambient air quality criterion (AAQC) in Ontario is 600  $\mu\text{g}/\text{m}^3$ . It should be noted that this value was not based on cancer effects at the time it was developed (1984). This value is still used today, and it serves as a basis for the calculation of the ½ hour Point of Impingement (½ h POI) value.

Occupational exposure guidelines have been developed for carbon tetrachloride. In the US, the Permissible Exposure Limit (PEL), established by the Occupational Safety and Health Administration (OSHA)<sup>11</sup> is 2 ppm (12400 ug/m<sup>3</sup>). The American Conference of Industrial Hygienists (ACGIH)<sup>6</sup> presently has a Threshold Limit Value-Time Weighted Average (TLV-TWA) of 5 ppm (31000 ug/m<sup>3</sup>) set to prevent liver effects, including cancer, fetal toxicity and teratogenesis.

The current Ontario occupational guideline for carbon tetrachloride is 5 ppm (31000 ug/m<sup>3</sup>). A new value, 12600 ug/m<sup>3</sup> (2 ppm) was recently proposed<sup>12</sup> based on a recent review of five jurisdictions, with the most stringent value having been selected.

The above guidelines for atmospheric carbon tetrachloride are summarized in Table 1 below.

## 2.2 Other Route Guidelines

There are no human studies regarding cancer effects after oral exposure to carbon tetrachloride. On the other hand, rodents fed carbon tetrachloride have developed liver tumors. It is generally assumed, in the context of guideline development, that humans also will develop tumors if carbon tetrachloride is ingested<sup>5</sup>.

Various guidelines and regulations are currently available for controlling the ingestion of carbon tetrachloride through drinking water. In fact, very little carbon tetrachloride is expected to be ingested through the consumption of food because of the low bioconcentration capability of this chemical, and of the low biomagnification that may occur in the food chain<sup>1</sup>.

As previously discussed, for the purpose of estimating cancer risks from oral exposures the US EPA<sup>5</sup> has established an oral slope factor of  $1.3 \times 10^{-1}$  (mg/kg-day)<sup>-1</sup>. This oral slope factor is the geometric mean of 4 different sets of results involving chronic gavage exposure of Syrian Hamsters, mice, and rats. By assuming a daily intake of 2 L of water and an average weight of 70 kg, the drinking water unit risk factor was estimated at  $3.7 \times 10^{-6}$  (ug/l)<sup>-1</sup>. Therefore, an incremental upper bound lifetime risk of 1 in one million of contracting liver cancer would be associated with daily consumption of 2 L of water contaminated with 0.3 ug/L (0.3 ppb) of carbon tetrachloride. Conversely, an excess risk of 1 in 100,000 would be associated with a concentration of 3 ug/L (3 ppb).

Several jurisdictions have based their water guidelines on the EPA methodology. However, very few have retained the concentration associated with an incremental cancer risk of 1 in 1,000,000 because of difficulties that may be encountered in the implementation and enforcement of this value. Hence, according to the most recent ATSDR document<sup>1</sup>, only the State of California has proposed the application of a permissible concentration in drinking water of 0.5 ug/L. The other jurisdictions cited, which include the states of Alabama, Arizona, Connecticut, Florida, Kansas, Maine, Massachusetts, Minnesota, New Jersey, Rhode Island and Vermont, all have permissible drinking water concentrations ranging from 2 to 5 ug/L. The tentative guideline for drinking water issued by the World Health Organization is also 3 ug/L.

The US EPA has also issued drinking water health advisories for the purpose of assessing short-term exposures only. These may not protect against cancer since they are generally higher than cancer-based guidelines and are intended primarily for emergency purposes.

The current Maximum Acceptable Concentration (MAC) in drinking water in Ontario is 5 ug/L based on toxicological, feasibility, and analytical considerations as summarized in the Canadian water quality guidelines handbook<sup>13</sup>. The above ingestion guidelines are summarized in Table 1.

TABLE 1. Summary of Exposure Guidelines for Carbon Tetrachloride from Leading Agencies

GUIDELINE APPLICATION	AGENCY(IES)	ORIGINAL VALUE	CONCENTRATION ("Original Form" converted to these -as applicable)			CALCULATED "ALLOWABLE" INTAKE (3)
			Unit Risk (1)	RsC (2) (1 x 10 <sup>-4</sup> )	ReC (2) (1 x 10 <sup>-4</sup> )	
INHALATION GUIDELINES						
Occupational	OSHA, ACCIH, Ontario	12400-31000 ug/m <sup>3</sup>	NA	NA	NA	248000 - 620000 (3.5 - 8.9)
Ambient Air Quality Guidelines	US states,	0.03-13 ug/m <sup>3</sup>	NA	NA	NA	0.6 - 260 (8.6 x 10 <sup>-4</sup> - 0.004)
Ontario Air Quality Guideline	OMOE/ARB	600 ug/m <sup>3</sup>	NA	NA	NA	12000 (0.17)
Chronic AELs/RfCs	CDHS, MDEP	2.4 - 86 ug/m <sup>3</sup>	NA	NA	NA	48 - 1720 (6.9 x 10 <sup>-4</sup> - 0.025)
Inhalation Cancer Potency Factor	EPA <sup>1</sup> CDHS	See Unit Risk column	1.5 x 10 <sup>-5</sup> 4.2 x 10 <sup>-5</sup>	0.7 0.24	0.07 0.024	for 1 x 10 <sup>-5</sup> risk: 4.8 - 14 (6.9 x 10 <sup>-5</sup> - 2 x 10 <sup>-4</sup> ) for 1 x 10 <sup>-6</sup> risk: 0.48 - 1.4 (6.9 x 10 <sup>-6</sup> - 2 x 10 <sup>-5</sup> )
INGESTION GUIDELINES						
Drinking Water Guideline	Ontario, WHO, US states	0.5 - 5 ug/L	NA	NA	NA	0.75 - 7.5 (1.0 x 10 <sup>-5</sup> - 1.0 x 10 <sup>-4</sup> )
Oral Cancer Potency Factor	EPA	1.3 x 10 <sup>-1</sup> (mg/kg-day) <sup>1</sup>	3.7 x 10 <sup>-4</sup> (US EPA)	2.7	0.27	for 1 x 10 <sup>-5</sup> risk: 4.0 (5.7 x 10 <sup>-5</sup> ) for 1 x 10 <sup>-6</sup> risk: 0.4 (5.7 x 10 <sup>-6</sup> )

<sup>1</sup>For inhalation and ingestion guidelines, unit risks are expressed as (ug/m<sup>3</sup>)<sup>-1</sup> and (ug/L)<sup>-1</sup>, respectively

<sup>2</sup>For inhalation and ingestion guidelines, risk specific concentrations are expressed as ug/m<sup>3</sup> and ug/L, respectively

<sup>3</sup>Intake was computed by assuming, where applicable, an adult weight of 70 kg, a breathing rate of 20 m<sup>3</sup>/day, a water intake of 1.5 L/day. In all cases 100% bioavailability of the intake was assumed.

<sup>4</sup>It should be noted that a 40% factor for pulmonary bioavailability is entrenched in the US EPA unit risk factor



### 3. HUMAN EXPOSURE ASSESSMENT

#### 3.1 Inhalation

##### 3.1.1 Ambient Air Quality

Ambient levels of carbon tetrachloride have been measured at five fixed site stations in Windsor by two monitoring agencies, the Ontario Ministry of Environment and Energy and the Environmental Protection Service of Environment Canada. The measurements include four years of data and includes 225 samples each collected over a 24 hour period. Concentration levels range from non-detectable to  $8.50 \text{ ug/m}^3$ , with the median, mean (average), 90th percentile and 95th percentile levels being 0.73, 0.65, 1.15 and  $1.28 \text{ ug/m}^3$ , respectively<sup>16</sup>.

It is possible to estimate the daily intake of carbon tetrachloride associated with these measures of Windsor ambient air quality, recognizing that personal real exposures/intakes may be quite different as further discussed in section 3.1.2. Table 2 below shows these estimated intakes for two different receptors, i.e., an adult and a child. It should be noted that these intakes were calculated based on 24 hour exposures and assume 100% bioavailability by the inhalation route.

Table 2. Estimated Daily Intakes of Carbon Tetrachloride Associated With Ambient Air Quality in Windsor

Air Quality Measure (a)	Concentration	Adult (b)	Child (b)
	$\text{ug/m}^3$	$\text{ug/day}$ ( $\text{ug/kg-day}$ )	$\text{ug/day}$ ( $\text{ug/kg-day}$ )
Median	0.73	14.6 (0.21)	3.7 (0.24)
Mean	0.65	13.0 (0.19)	3.3 (0.22)
90th percentile	1.15	23.0 (0.33)	5.8 (0.38)
a) Based on 225, 24 hour average samples b) Assuming the following weights and inhalation rates per day (ie. per 24 hour period): Adult: 70 kg; $20 \text{ m}^3/\text{day}$ Child: 15 kg; $5 \text{ m}^3/\text{day}$			

##### 3.1.2 Microenvironments

It is reasonable to assume that the daily carbon tetrachloride intakes associated with typical personal exposure patterns can be better estimated from various microenvironmental concentrations than from fixed site monitoring data. For the purpose of scoping population exposures, the set of typical receptors in Table 3 below was considered. Examples of the receptor types and/or their characteristics are also included in Table 3. Using carbon tetrachloride concentrations acquired in various microenvironments, either as part of the personal exposure or subsequent microenvironment study in Windsor, it is possible to scope out various typical personal inhalation exposure scenarios for the above receptors. The estimated



daily intakes (in ug/day) of these receptors are summarized in Table 4.

Table 3. Receptors With Typical Personal Exposure Patterns

NAME OF RECEPTOR TYPE	CHARACTERISTICS	NAME OF RECEPTOR TYPE	CHARACTERISTICS
Average Office Worker (Non-smoking)	Eg. - Typical office worker (Based on Windsor volunteers and US EPA TEAM study; not smoking at home)	High Outdoor Receptor	Eg. - Construction workers; - Bicycle couriers - Police - Long distance runners
Average Office Worker (Non-smoker in a Smoker Environment)	Eg. - Typical office worker (Based on Windsor volunteers and US EPA TEAM study; smoking at home)	High Indoor Receptor	Eg. - 'Shut-ins'- Invalids - Elderly, non-mobile
Average Youth	Eg. Special exposures at shopping malls and athletic facilities (pools) in addition to school;	High Commuting Receptor	Eg.- Bus drivers - Taxi drivers - Delivery/ Distribution Services
Average Child (Non-Smoker Home & No Exposure to Tobacco Smoke)	Eg. Similar to average office worker except 'School' replaces 'Office';	Active Receptor # 1	Eg.- 7 hr/week in Bingo Hall or Bar
Average Child (Non-Smoker Home & Typical Exposure to Tobacco Smoke)	Eg. Includes typical times that children may be in proximity to tobacco smoke, outside the home, based on activity pattern studies;		
Average Child (Smoker Home with Exposure to Tobacco Smoke)	Eg. Child living in a house where there is a smoker		

A microenvironment, in which measurements were not taken, is the bathroom during bathing and showering.

Volatile organic chemicals will partition from the hot water during showering and bathing and be inhaled by the person in the bathroom. A simple one-compartment model has been developed that takes into account the air exchange between shower stall and bathroom and the rest of the house and calculates the maximum concentration -  $C_{max}$  - reached during showering<sup>15</sup>. The formula is

Table 4. Estimated Daily Intakes (ug/day) Associated with Typical Personal Exposures (See footnote 1.)

MICRO ENVIRONMENT	Air Concentration (ug/m <sup>3</sup> ) (h)	Average Office Worker	Average Office Worker	Youth	Average Child	Average Child	Average Child	High Outdoor Receptor	High Indoor Receptor	High Commuting Receptor
		Non-smoker	Smoker Home Environment		Non smoker home/No exposure to tobacco smoke	Non smoker home/Typical exposure to tobacco smoke				
		Time spent (hrs)	Time spent (hrs)	Time spent (hrs)	Time spent (hrs)	Time spent (hrs)	Time spent (hrs)	Time spent (hrs)	Time spent (hrs)	Time spent (hrs)
Office	3.6/11.7 (m)	6.7(a)	6.7(a)				1.7			
School	3.6/11.7 (d)			6.7	6.7	6.7				
Home	3.1/5.2 (m)			13.3	13.7	12.4	13.7	20.4		13.7
Commuting (in-transit)	6.6/15.2 (m)	1.0(a)	1.0(a)	1.0(f)	1.0(f)	1.0(f)	1(a)	1(a)	1(a)	7.7
Urban (Outdoors)	0.7/ 1.2	2.6(a)	2.6(a)	2.6	2.6	2.6	7.6(g)	2.6		2.6
Home with smokers	4.4/9.4 (c)		13.7(b)			1.3(e)				
Shopping Mall/Market	3.6/11.7 (n)	0.4(i)		0.4(i)						
Bar or Bingo Hall	7.3/18.7 (k)									
INTEGRATED EXPOSURE (ug-hrs/m <sup>3</sup> )		75.2/ 170.6	92.8/ 225.5	75.2/ 170.6	75.0/ 168.0	76.7/ 173.4	60.5/ 115.5	71.7/ 124.4		95.1/ 191.4

TIME WEIGHTED AVERAGE EXPOSURE (ug/m <sup>3</sup> over 24 hr) (h)	3.1/7.1	3.9/9.4	3.1/7.1	3.1/7.0	3.2/7.2	2.5/4.8	3.0/5.2	4.0/8.0
INTAKE/DAY (UG/DAY) (h)	62.7/142.1	77.4/188.0	43.9/ 99.5	15.6/35.0	16.0/36.1	50.4/96.2	59.7/ 103.7	79.3/159.5

### Estimations:

\* INTEGRATED EXPOSURE (ug-hrs/m<sup>3</sup>) = SUM OF [Microenvironment concentration x Time spent in Microenvironment]

\* TIME WEIGHTED AVERAGE EXPOSURE (ug/m<sup>3</sup>) = INTEGRATED EXPOSURE/24 hr

\* INTAKE/DAY (ug/day) = TIME WEIGHTED AVERAGE EXPOSURE x DAILY BREATHING RATE (ie. for Adult or Youth or Child as applicable)

### Footnotes:

- a.) TIME BUDGET ANALYSIS: Windsor '91 Summer PEP Study; Handout to Volunteers; May/92 (R. Bell)
- b.) Sum of 'Indoor, Home' and 'Indoor Other' in a.)
- c.) Although carbon tetrachloride is normally not specifically associated with tobacco smoke, these values were obtained during the personal exposure study in Windsor from homes where smoking was permitted.
- d.) Assumed to be same 'microenvironment' concentration that were measured by PEP study in the 'Office' environment.
- e.) Average time spent in proximity to tobacco smoke, in various locations outside the home, was approximately 1.3 hours, based on a study of children's activity patterns; (Ref: Study of Children's Activity Patterns, State of California, Air Resources Board, Contract No. A 733-149). Assume that benzene concentrations, when in proximity to tobacco smoke is represented by the median levels referenced in footnote "c," above.
- f.) Assume 1 hour is spent in the car per day.
- g.) For the 'high-outdoor' receptor, urban outdoor concentrations were assumed to be represented by the 'mean' and 90th percentile concentrations taken from the fixed site monitoring network. Also assume that for this group, the 6.7 hours of 'at work' exposure is divided so that 1.7 hours is spent in the office and 5 hours is added to the 2.6 hours of urban outdoor exposure for a total of 7.6 hours.
- h.) First number is the 'mean'. The second number is the 90th percentile, if available; otherwise it is the maximum value measured.
- i.) Assumed that approximately 2.8 hours per week are spent on malls shopping; this was distributed over seven days yielding '0.4 hours/day' in malls.
- j.) Assumed that this receptor spends approximately 7 hours per week in a bingo hall or bar; this was distributed over seven days yielding '1 hr/day' in bingo halls or bars.
- k.) 'Bar' and 'bingo halls' data were combined to obtain these values and these were assumed to be representative of both of these microenvironments.
- l.) Two additional typical personal exposure patterns that were evaluated but are not shown in detail in this table are the 'Average Child in a Smoker Home' and the 'Active Receptor # 1' as noted in Table 3 above. The corresponding intakes/day (ie. mean/90th percentile) for these two receptors are 19.3/47.0 and 66.0/151.2, respectively.
- m.) The 'mean' and '90th percentile' concentrations for the 'Office', 'Home' and 'Commuting' microenvironments were derived from the Summer 1991 and Winter 1992 personal exposure studies in Windsor. For the 'office' microenvironment the two values represent the minimum and maximum values, since there were insufficient detectable values to calculate a mean.
- n.) Carbon tetrachloride was not detected at the 'market' in the 2 samples that were taken. It was assumed that the 'Sh. mall/Market' microenvironment can be represented by the same concentration as that of the 'Office' microenvironment.

$$C_{amax} = C_w f F_w t_d / V_a$$

where:  $C_w$  is the water concentration (ug/L)  
 $f$  is the fractional volatilization rate with an assumed value of 0.75 (range 0.5 - 0.9)  
 $F_w$  is the volume of water used (L/h)  
 $t_d$  is the time spent in the shower or bath (h)  
 $V_a$  is the volume of the shower stall or bathroom (L)

The shower stall is assumed to have a volume of 2 m<sup>3</sup> or 2000 L and the showering time is 0.25 h. The average flow rate is 260 L/h and the maximum is 720 (12). The estimated water concentration is 0.1 ug/L (s.1.3.2.2). The maximum concentration is, on the average, 2.4 ug/m<sup>3</sup> and the upper limit is 6.8 ug/m<sup>3</sup>.

The average concentration is approximately half that of  $C_{amax}$  (assuming a linear increase with time). The average inhalation rate is 20 m<sup>3</sup>/d or 833 L/h. The average amount inhaled during the showering is then 0.26 ug and the maximum is 0.70 ug.

An alternative scenario as described by the authors assumes full exchange between the shower stall and the bathroom ( $V_a$  - 10m<sup>3</sup>), 15 minutes for a shower and an additional 15 minutes in the bathroom. The concentration during the shower is  $C_{amax}/2$  and during the remaining 15 minutes is approximately  $C_{aav}$  (assuming the exchange with the rest of the house is slow). Under these circumstances,  $C_{amax}$  is 0.49, with a maximum value of 1.35 ug/m<sup>3</sup> and the amounts inhaled are 0.15 and 0.42 ug. These calculations assume that 100% of the inhaled CCl<sub>4</sub> is absorbed across the lung. The actual absorption is about 60% (Ref. 1, p.36).

In view of the relatively small intake from this microenvironment as compared to other inhalation intakes, this can be considered negligible.

In order to place the above inhalation exposures (ie. intakes) in Windsor in perspective, it is appropriate to compare them to daily intakes of people who smoke.

### 3.1.3 Smoking.

Although studies have shown that CCl<sub>4</sub> is a common contaminant of indoor air and that concentrations indoors are usually higher than outdoors, the source of the chemical appears to be building materials and products, such as pesticides and cleaning agents(Ref. 1, p.78). It does not appear to be linked to smoking.

Furthermore it is also important to place the inhalation exposures(ie. intakes) in Windsor into perspective, relative to general exposures from other media (ie. see section 3.2).

## 3.2 Other Routes

### 3.2.1 Ingestion of Food

Estimates of the carbon tetrachloride uptake\* from foods are given in table 5-2\* of ATSDR (Ref. 1, p.80). To arrive at the uptake values, the minimum and maximum levels of carbon tetrachloride in foods were multiplied by the minimum and maximum worldwide food consumption for individuals for each food category.

\* The table in Ref. 1 labels the exposures "uptake", which implies that bioavailability has already been taken into account.



The totals for all food supplies are:

minimum	0.21 mg/y	0.58 ug/d
average	1.12	3.1
maximum	7.33	20.0

The major sources are meats, vegetables and fruits and milk products for the maximum exposure. Carbon tetrachloride does not appear to occur in significant quantities in other food groups. The milk products group has a 1000-fold range of exposures. Since the maximum exposure is the product of maximum food intake and maximum concentration, the percentage of the population with this exposure is likely to be small and the average exposure is likely a more realistic estimate.

Assuming that the exposures above are for adults, the exposure for children can be calculated by multiplying the adult exposures by the ratio (intake by children for a food group/intake by adults for same food group) and adding the exposures. The food intakes for children 5-11 y and adults 40-64 y were taken from Dabeka *et al* (1993)<sup>14</sup>. The resulting exposures for children 5-11 y are:

minimum	0.17 mg/y	0.47 ug/d
maximum	5.9	16.3

This assumes that the children and adults have the same diets. It was not possible to calculate the average intake for children from the ATSDR data. These exposure figures are from a 1978 publication and may no longer be applicable, since "levels in most foods are below analytical detection limits"(Ref. 1, p 79).

No studies on absorption from the gastrointestinal tract in humans after oral exposure were located (Ref. 1, p 36). Animal studies indicate that CCl<sub>4</sub> is rapidly and extensively absorbed from the gastrointestinal tract as 80-85% of an oral dose may be recovered in expired air, indicating that the absorption is at least 85%

### 3.2.2 Drinking Water

The treated drinking water in Windsor was analyzed by the Laboratory Services Branch of the MOE for benzene 8 times in 1990 and 1991, with a detection limit of 0.2 ug/L. All concentrations were less than the detection limit. The average concentration is assumed to be one-half of the detection limit or 0.1 ug/L. This is consistent with studies in the USA that 99% of all groundwater supplies and 95% of all surface samples contain <0.5 ug/L.

The amount of CCl<sub>4</sub> ingested is then, based on the liquid ingestion volumes in the drinking water survey of Health and Welfare Canada<sup>17</sup>.

-	adult median (1.49 L/d):	0.15 ug/d
	90th percentile (2.59 L/d):	0.26 ug/d
-	child: median (0.76 L/d):	0.08 ug/d
	90th percentile (1.5 L/d):	0.15 ug/d

### 3.2.3 Soil

There are no analyses for carbon tetrachloride in the soils at Windsor. ATSDR (Ref. 1, p.78) suggests that, because  $\text{CCl}_4$  is ubiquitous in air, it is likely that trace levels of carbon tetrachloride are present in the surface soils around the globe. In the absence of any data, however, the intake from soil cannot be calculated.

### 3.2.4 Dermal

#### 3.2.4.1 During Showering and Bathing

EPA (Ref. 18, p. 5-49 *et seq*) has proposed a model for transient state dermal adsorption from water. The basic formula is, for  $t < t^*$

$$DA_{\text{event}} = 2K_p C_v (6\tau t_{\text{event}} / \pi)^{1/2}$$

where:  $DA_{\text{event}}$  is dose absorbed per unit area per event ( $\text{mg}/\text{cm}^2 \cdot \text{event}$ )

$K_p$  is the permeability coefficient ( $\text{cm}/\text{hr}$ )

$C_v$  is the concentration in the water ( $\text{mg}/\text{cm}^3$ )

$t_{\text{event}}$  is the time spent showering or bathing ( $\text{hr}$ )

$\tau$  is a number calculated from the skin thickness and diffusivity of the chemical in the skin ( $\text{hr}$ )

$t^*$  is number that is calculated from the value of  $B$  ( $\text{hr}$ ) ( $B = K_{ow}/10^4$ ;  $K_{ow}$  is the octanol/water partition coefficient)

Table 5-8 of reference 18 gives the appropriate values (estimated  $K_p = 0.022 \text{ cm/hr}$ ;  $\tau = 0.76 \text{ hr}$  and  $t^* = 1.8 \text{ hr}$ ) to use in the above equation and assuming that a shower takes 0.25 hr/day and a bath 0.5 hr and a median skin surface area of 19400  $\text{cm}^2$  (Ref. 18; table 8-3) for an adult and a water concentration of 0.1  $\text{ug}/\text{L}$  (or  $0.1 \times 10^{-6} \text{ mg}/\text{cm}^3$ ) (s. 3.2.2), the amount absorbed during a shower is 0.005  $\text{ug}$  and during a bath, 0.01  $\text{ug}$ . For a child, with median skin surface area of 7310  $\text{cm}^2$ , the amounts absorbed are 0.002 and 0.004  $\text{ug}$ .

#### 3.2.4.2 Contact With Soil and Dirt

As was pointed out in s. 3.2.3, there is no data on the concentration of carbon tetrachloride in the soil in Windsor. It is not possible, therefore, to estimate the dermal uptake from contact with soil and dirt.

#### 3.2.4.3 From Carbon Tetrachloride Vapour in the Air

The absorption through the skin of vapors in the air can be calculated from the formula proposed by the US EPA (Ref. 18; p. 7-16 *et seq*)

$$DA_{\text{event}} = K_p^{air} C_{air} t_{\text{event}}$$

where

$DA_{event}$  is the absorbed dose per event (mg/cm<sup>2</sup>-event)

$K_p^{air}$  is the permeability constant (cm/hr)

$C_{air}$  is the concentration of the vapor in air (mg/cm<sup>3</sup>)

$t_{event}$  is the exposure time (hr/event)

The value estimated from the fat/air partition coefficient for the permeability coefficient of carbon tetrachloride is 0.137 cm/hr (Ref. 18; table 7-7).

From the scenarios in s. 3.1.2, a reasonable range in weighted air concentrations is 2.5 (median) to 9.5 ug/m<sup>3</sup>. The median surface area for an adult is 1.94 m<sup>2</sup> and for a child, 0.73. The exposure time is 24 hrs.

Using the range of the concentrations, the doses absorbed per day are

adult : 0.2 to 0.6 ug

child: 0.06 to 0.2 ug

#### 4. RISK CHARACTERIZATION AND PERSPECTIVES

Exposures, expressed as daily intakes in units of ug/day, were assessed in section 3. Inhalation, ingestion and dermal routes of exposure were considered. Table 5 below summarizes the daily intakes (or ranges of daily intakes) of carbon tetrachloride, for adults and children, estimated in section 3. It should be noted that in section 3, the intakes for inhalation and sometimes for ingestion assumed 100% bioavailability. The intake for dermal exposures are amounts absorbed systemically and hence already include bioavailability considerations. Table 5 has two columns for both adults and children. The first set of columns (ie. '100 % Bioav') give the intakes with 100 % bioavailability having been assumed; the second set (ie. "Bioav. Incl."), gives intakes for which bioavailability has been taken into consideration (ie. if information was available as noted in the footnotes). This second set of columns should give a better picture of the relative importance of various exposure routes. As far as comparison to exposure guidelines and intakes associated with cancer risk, the intakes in the first set of columns of Table 5 will be used since the exposure guidelines are also expressed as intakes for which we have assumed 100 % bioavailability.

To characterize risks, the various exposure guidelines discussed in Section 2 are compared to the estimated exposures from inhalation and other routes as discussed in Section 3. Because of the assumptions, uncertainties and ranges of values available from both exposures (see Table 5) and the various exposure guidelines (see Table 1), risk characterization is most appropriately done by comparison of ranges of values.

Table 6 below provides a graphic representation of this comparison of exposures, exposure guidelines and intakes associated with inhalation cancer risk, based on ug intake/day (ie. 'INTAKE in Micrograms per day' increasing upwards on the vertical scale).

The middle section of Table 6, "Exposures", depicts the exposures calculated in Section 3, expressed as

intake/day (ie. ug/day). The exposures depicted are: *Outdoor Air Quality* - the exposure from spending 100 % of the day outdoors; *Typical Outdoor Exposure* - the exposure from three hours only outdoors, provided for perspective on the contribution to risk solely from contaminants present in outdoor air; *Typical Personal Exposures* - the range of exposures associated with ten different exposure scenarios, combining periods of indoor, outdoor and various microenvironment exposures. Exposure scenarios are included for adults and children, assuming 20 and 5 m<sup>3</sup>/day inhalation rates respectively. For 'outdoor air quality' (ie. 100% outdoor exposure), for 'typical outdoor exposures' (ie. 3 hr), and for the 'typical activity patterns' the ranges shown, bracket the lowest mean to the highest 90th percentile.

The left section of Table 6, "Exposure Guidelines", expresses the various guidelines discussed in Section 2 in terms of calculated "allowable" intake/day for adults and children. The values are taken from Table 1. Within each type of guideline group (eg. outdoor air) ranges of exposure guidelines, when available, are indicated. Thus, ranges of Air Quality Guidelines (ie. 'Outdoor Air'), Occupational guidelines (ie. 'Workplace Air'), and chronic health effects based reference concentrations (ie. 'Chronic AEL') are shown. The existing MOEE guideline for carbon tetrachloride is also shown as a horizontal bar. Comparison of "Exposure Guidelines" to "Exposures" should be done with care. For example, occupational guidelines are included for perspective purposes only. For caveats regarding this comparison see section 4.1.1 of the main report.

The right section of Table 6, "Intakes Associated With Cancer Risk", shows the intakes associated with different levels of cancer risk. Ranges of carcinogenic risk levels (associated with  $1 \times 10^{-5}$  risk and  $1 \times 10^{-6}$  risk) are depicted. Comparison of "Exposures" to "Intakes Associated With Cancer Risk" is appropriate for adult exposures only, since cancer risk estimates apply to a lifetime of exposure and people are adults for the majority of their lives. Adult exposures in the bars of the "Exposure" section fall in the top 70 % of the bars which represent exposures of adults and children.

Based on the tabular analysis (Table 5) and the graphic risk characterization (Table 6), the following observations and deductions can be made:

#### Health messages:

1) It is apparent, that the inhalation route is generally higher than other exposure routes for carbon tetrachloride. Exposure by ingestion and via the skin are less, especially if one takes into consideration the facts that very few persons are expected to be exposed at the maximum levels from food (ie. as implied by the maximum value shown in Table 5) and that the average intake from food is  $\approx 3.1$  ug/day (see note 'd' and the 'Avg.' value of 3.1 indicated in Table 5). Dermal exposure appears to be lowest in importance.

2) All the inhalation exposures associated with outdoor air quality (ie. 100 % outdoor exposure) and with typical outdoor exposure (ie. 3 hr) are less than the range of available chronic acceptable exposure levels (ie. range is 48 - 1720 ug/day) proposed by California (CDHS) and Massachusetts (MDEP). However, some of the exposures associated personal activity patterns fall in the lower 10% range of these chronic acceptable exposure levels. These chronic acceptable exposure levels are considered to be purely health based and are protective against all chronic health effects other than cancer risk. Therefore, the possibility of long-term health effects, other than cancer risk, is unlikely with all inhalation exposures, and possible for some exposures associated with personal activity patterns.

This comparison of exposures to chronic acceptable exposure levels can also be expressed more quantitatively in the form of a hazard index. These hazard index comparisons for all substances are summarized and are found in section 4.1.5 of the main report.



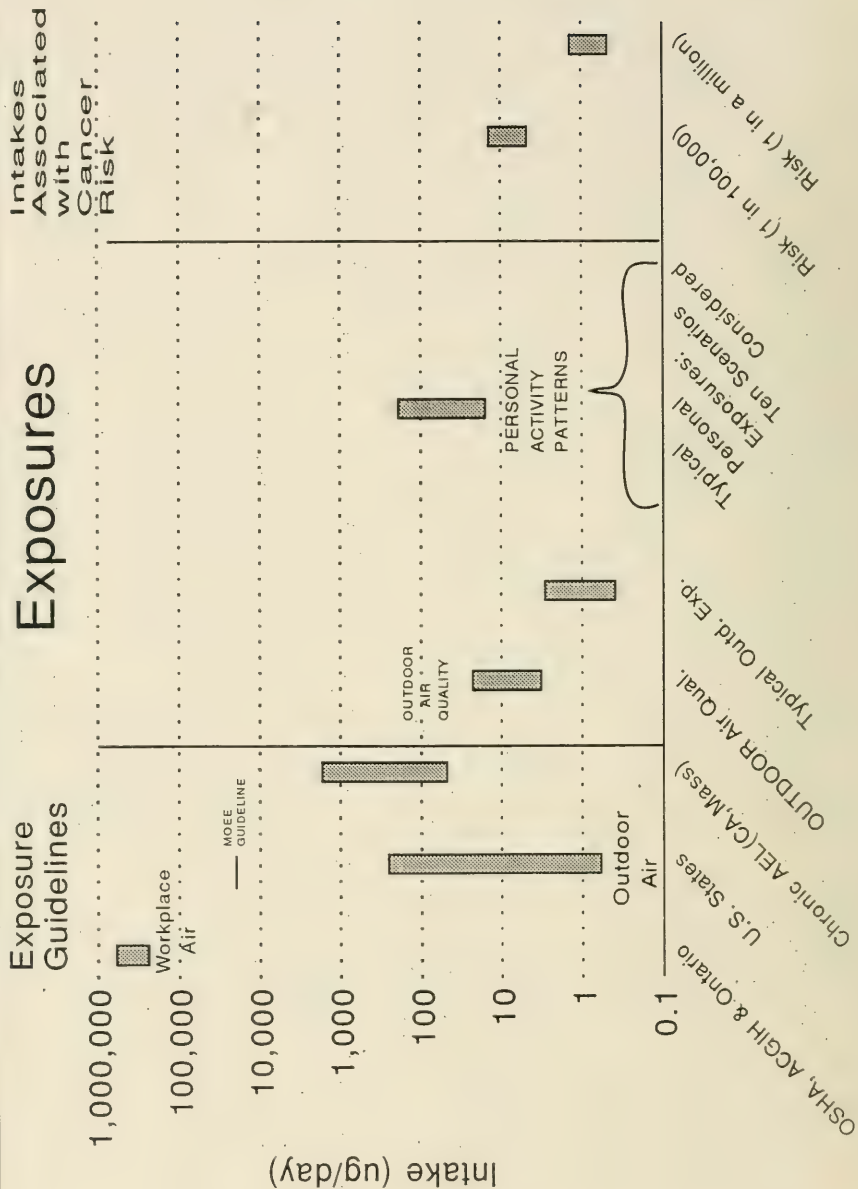
**Table 5. Summary of Estimated Daily Intakes and/or Range of Intakes (in ug /day), from Various Exposure Pathways (ie. intakes, assuming 100 % bioavailability and intakes with bioavailability taken into consideration)**

EXPOSURE PATHWAY		ADULT ug/day  (100 % Bioav.)	ADULT ug/day  (Bioav. Incl.)	CHILD ug/day  (100 % Bioav.)	CHILD ug/day  (Bioav. Incl.)
INHALATION	Outdoor Air Quality - Windsor (ie. 100 % outdoor exposure)(a)	13 - 23	5.2 - 9.2 (f)	3.3 - 5.8	1.3 - 2.3 (f)
	Typical outdoor exposure (ie. = 3hr)(b)	1.6 - 2.9	0.6 - 1.2 (f)	0.4 - 0.7	0.2 - 0.3 (f)
	Typical personal exposures(ie. Table 4) (c)	50.4 - 187.9	20.2 - 75.2 (f)	15.6 - 47.0	6.2 - 18.8 (f)
	Smoking (e)	-	-		
INGESTION	Food (d)		0.58 - 20 (Avg. 3.1) (d)		0.17 - 16
	Drinking water (d)	0.15 - 0.26	0.12 - 0.21	0.08 - 0.15	0.06 - 0.12
	Soil (g)	-	-	-	-
	TOTAL (Ingestion)		0.7 - 20.2		0.23 - 16.1
DERMAL	During showering		0.005 - 0.01		0.002 - 0.004
	Contact with soil & dirt (g)		-		-
	From carbon tetrachloride vapour in the air		0.2 - 0.6		0.06 - 0.2
	TOTAL (Dermal)		0.2 - 0.6		0.06 - 0.2
<p>a.) Range of intakes is <u>associated with</u> the range of the 'mean' to '90th percentile' concentrations in outdoor air. It is to be noted that people are not exposed 24 hours to <u>outdoor</u> air. This estimation assumes 100 % exposure to outdoor air and is a measure of outdoor air quality per se and not of actual exposure.</p> <p>b.) Range of intakes <u>calculated from</u> the 'mean' to '90th percentile' concentrations in outdoor air and assuming a 'typical' outdoor air exposure of = 3 hr(ie. corresponding to breathing 2.5 m<sup>3</sup>/3hr for adults and 0.63 m<sup>3</sup>/3hr for children.</p> <p>c.) Range of intakes is estimated from the range of the lowest 'mean' and the highest '90th percentile' concentrations obtained from personal exposure and microenvironment measurements.</p> <p>d.) The bioavailability from ingested water and food is estimated to be 80% (s. 1.1). The exposures from food are labelled "uptake" in Ref. 1, implying that bioavailability has already been taken into account. In addition, the highest values are derived by multiplying the maximum concentration in a particular food group with the maximum consumption of that food group. Very few persons are expected to be exposed at this level. The average intake from food for adults is 3.1 ug/d (see s. 3.2.1).</p> <p>e.) Carbon tetrachloride is not produced during smoking (s. 3.1.3)</p> <p>f.) The amount absorbed in the lung is 40 % (s. 1.1)</p> <p>g.) There appears to be no data that would allow calculations of these exposure pathways. It is expected that any exposures would be small compared to the other pathways (s. 3.2.3).</p>					



Table 6. CARBON TETRACHLORIDE RISK CHARACTERIZATION in WINDSOR  
 Ranges of exposure guidelines, exposures and risk estimates  
 (Inhalation unless otherwise specified)

TABLE 6.1



3) The most conservative range of available exposure guidelines are depicted in Table 6 under Intakes Associated with Cancer Risk. These guidelines were proposed by CDHS, and the US EPA. As shown in Table 6, they overlap with and are exceeded by the estimated exposures. Because people are adults for the majority of their lives, these intakes associated with cancer risk are depicted for adults only. The inhalation intakes for adults associated with 'outdoor air quality' (ie. 100 % outdoor exposure), 'typical outdoor exposure' (ie. 3 hr) and 'typical personal exposures' range between 13 - 23 ug/day, 1.6 -2.9 ug/day and 50.4 - 187.9 ug/day, respectively (from Tables 2, 4 and 5). These intakes and the corresponding doses in mg/kg-day are summarized in Table 7. As noted previously (see s. 2.1.2), the EPA unit risk value already includes a 40% absorption assumption, while the CDHS unit risk does not. For this reason, when calculating risks from the CDHS value, the daily intakes were adjusted for 40% absorption (see footnote b in Table 7). Using the various potencies from the two agencies, the range of risks associated with 'outdoor air quality' (ie. 100% outdoor exposure) is between  $1.0 \times 10^{-5}$  and  $2.0 \times 10^{-5}$ . Similarly the range of risks associated with 'typical outdoor exposures' (ie. 3 hr) is between  $1.2 \times 10^{-6}$  and  $2.5 \times 10^{-6}$ . Similarly the range of risks associated with 'typical personal exposures' is between  $3.9 \times 10^{-5}$  and  $1.6 \times 10^{-4}$ . The risks associated with 'typical personal exposures' are slightly higher than the risks associated with 'outdoor air quality' which in turn is higher than 'typical outdoor exposures'. This range of risk analysis is summarized in Table 7. It should be further noted, that this risk characterization (ie. using carcinogenic risk based limits) is based on an assumed lifetime exposure (ie. 24 hours, every day, for 70 years) and hence is a very conservative assumption.

**Table 7. Range of Inhalation Cancer Risks Associated with Estimated Intakes (ie. for adult exposures only) of Carbon Tetrachloride**

RANGE of INHALATION INTAKES			POTENCY (a)		RANGE of RISKS
Environment	Unit ug/day	Unit mg/kg/day	Agency	Unit (mg/kg-d) <sup>1</sup>	
OUTDOOR AIR QUALITY (Windsor)	13 - 23	$1.9 \times 10^{-4}$ - $3.3 \times 10^{-4}$	EPA	$5.4 \times 10^{-2}$	$1.0 \times 10^{-5}$ - $1.8 \times 10^{-5}$
			CDHS	$1.5 \times 10^{-1}$	$1.1 \times 10^{-5}$ - $2.0 \times 10^{-5}$ (b)
			WHO	NA	
			OVERALL RANGE OF RISKS: $1.0 \times 10^{-5}$ - $2.0 \times 10^{-5}$		
TYPICAL OUTDOOR EXPOSURE (ie.= 3 hr.)	1.6 - 2.9	$2.3 \times 10^{-5}$ - $4.1 \times 10^{-5}$	EPA	$5.4 \times 10^{-2}$	$1.2 \times 10^{-6}$ - $2.2 \times 10^{-6}$
			CDHS	$1.5 \times 10^{-1}$	$1.4 \times 10^{-6}$ - $2.5 \times 10^{-6}$ (b)
			WHO	NA	
			OVERALL RANGE OF RISKS: $1.2 \times 10^{-6}$ - $2.5 \times 10^{-6}$		
TYPICAL PERSONAL EXPOSURES	50.4 - 187.9	$7.2 \times 10^{-4}$ - $2.7 \times 10^{-3}$	EPA	$5.4 \times 10^{-2}$	$3.9 \times 10^{-5}$ - $1.5 \times 10^{-4}$
			CDHS	$1.5 \times 10^{-1}$	$4.3 \times 10^{-5}$ - $1.6 \times 10^{-4}$ (b)
			WHO	NA	
			OVERALL RANGE OF RISKS: $3.9 \times 10^{-5}$ - $1.6 \times 10^{-4}$		
a. These are equivalent potency factors calculated from the unit risks proposed by the agencies listed; assumed adult weight of 70 kg and 20 m <sup>3</sup> per day.					
b. Intakes were adjusted for 40 % absorption when calculating risks from the CDHS equivalent potency factor. This makes the CDHS risk estimates comparable to the EPA estimates since the EPA unit risk value already includes a 40 % absorption assumption.					

- 4) Carbon tetrachloride exposure from smoking is not expected to be significant.
- 5) Considering the information in Table 5, the exposures from the *non-inhalation* pathways are:
- *Ingestion* of food and water:

adult - 0.7 to 20 ug/day  
child - 0.2 to 16 ug/day

It should be noted that these values are most likely 6-fold less, since the average intake from food is  $\approx 3.1$  ug/day.

- *Dermal* absorption:

During showering and bathing:

- adults: 0.005 to 0.01 ug/d
- child: 0.002 to 0.004 ug/d

From carbon tetrachloride vapour in the air:

- adult: 0.2 to 0.6 ug/day
- child: 0.06 to 0.2 ug/d

These ingestion and dermal exposures are several times less (ie. especially if the average rather than the maximum intake from food is considered - Table 5, footnote 'd' and section 3.2.1) than from inhalation. The risk associated with these exposures (ie. using the average intake from food) are  $\approx 1 \times 10^{-5}$  and therefore they can add to the cancer risk associated with carbon tetrachloride.

#### Regulatory compliance messages:

- 6) The risk characterization in Table 6 indicates that, for the inhalation receptor exposures considered:
- The exposures potentially associated with outdoor air quality, for adults, youth and children, fall in the lower 10% range of the air quality guidelines of various jurisdictions.
  - Exposures associated with typical outdoor exposure (ie. 3 hr) fall in the lower 1 % range of the air quality guidelines of various jurisdictions
  - Exposures associated with personal activity patterns fall in the lower 75% range of the air quality guidelines of various jurisdictions.

It should be noted that these air quality guidelines may be of different types. Some are purely health based and some are regulatory and therefore may have been influenced by various risk management considerations. The regulatory guidelines may also have different uses (eg. judging the acceptability of air quality per se or judging the incremental addition by a source to the existing air quality).

- 7) Table 6 also indicates that all the inhalation exposures are less than the range of occupational levels.
- 8) The ingestion intake also falls within (ie. especially if the average rather than the maximum intake from food is considered) the drinking water guidelines of Ontario, WHO and various U.S. states (ie. 0.75 - 7.5 ug/day, from Table 1).
- 9) MOEE will be reviewing the basis of the existing standard for carbon tetrachloride.

#### Summary and recommendations:

- ♦ All the inhalation exposures, except some personal exposures associated with commuting and indoor environments, are less than the range of available chronic acceptable exposure levels. Therefore, the possibility of long-term health effects, other than cancer risk, is unlikely with all inhalation exposures, and possible for some exposures associated with personal activity patterns.
- ♦ The range of estimated inhalation risks associated with 'outdoor air quality' (ie. 100% outdoor exposure) is between  $1.0 \times 10^{-5}$  and  $2.0 \times 10^{-5}$ . Similarly the range of risks associated with 'typical personal exposures' is between  $3.9 \times 10^{-5}$  and  $1.6 \times 10^{-4}$ . Since these levels of risk exceed  $1 \times 10^{-5}$ , a level generally deemed to be negligible, it is recommended that carbon tetrachloride be considered a candidate for reduction of exposure.
- ♦ Exposures and therefore risks associated with 'typical personal exposures' are slightly higher than the risks associated with 'outdoor air quality'.
- ♦ The commuting and some indoor environments are the most dominant in the upper range of 'typical personal exposures'. Carbon tetrachloride exposure from smoking is not expected to be significant.
- ♦ Ingestion and dermal exposures are several times less (ie. especially if the average rather than the maximum intake from food is considered) than from inhalation. The risk associated with these exposures (ie. using the average intake from food) are  $\approx 1 \times 10^{-5}$  and therefore they can add to the cancer risk associated with carbon tetrachloride.

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**APPENDIX 4**  
**RISK ANALYSIS FOR FORMALDEHYDE**



APPENDIX 4  
RISK ANALYSIS FOR FORMALDEHYDE

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## FORMALDEHYDE

### DESCRIPTION and SOURCES OF FORMALDEHYDE.

Formaldehyde is a colorless gas at normal temperatures with a pungent, irritating odour. It is used in the manufacture of several types of resins (eg. urea-formaldehyde, phenol-formaldehyde). These resins are used in a wide variety of pressed-wood products, such as plywood, particle board and counter tops. It is also a raw material in the production of urea.

In addition, formaldehyde is produced as a byproduct in several types of processes. These include combustion sources (ie. mobile, stationary and natural sources). Formaldehyde is the most prevalent aldehyde in vehicle exhaust. Gas ranges and space heaters emit formaldehyde indoors. Other processes, in which formaldehyde is a byproduct, are petroleum refinery catalytic cracking and coking, asphaltic concrete production, and atmospheric photooxidation of unburned hydrocarbons.

### 1 HAZARD IDENTIFICATION

Several reviews and secondary sources of information on the toxicology, epidemiology, environmental fate, and properties of formaldehyde are available in the open literature<sup>1-7</sup>. These reviews generally encompass past and recent findings obtained from detailed literature search, and they provide an excellent integrative and interpretative evaluation of the formaldehyde issue as related to its potential health effects on humans following exposure through various environmental pathways. As it is the scope of the current document to provide a general, although comprehensive updated overview on the toxicology of formaldehyde, excerpts of these reviews were used in the following sections to summarize the information considered to be of relevance for the Windsor study. For a more detailed discussion of the health effects of formaldehyde, the reader is referred to the references contained in section 5.

#### 1.1 Absorption and Metabolism

Formaldehyde is a gas at standard conditions of temperature and pressure and, consequently, the main route of human exposure is through inhalation of contaminated air, especially in indoor environments. Ingestion of contaminated food and, to a lesser extent, of drinking water may also contribute significantly to total human exposure depending on the physical or chemical form of formaldehyde. Approximate total uptakes of formaldehyde estimated by the World Health Organization<sup>6</sup> for the inhalation and oral routes are of 1-2 mg/day and 1.7-14.2 mg/day, respectively. WHO notes, however, that most of the formaldehyde in food, which contributes for more than 80% of the oral uptake, is bound and unavailable for absorption.

Due to its water solubility, formaldehyde is readily absorbed and/or reacts in the upper part of the respiratory tract where rates as high as 100% have been measured in animals. Absorption through the gastrointestinal mucosa may be as important as in the respiratory tract, while dermal uptake appears to be very slight<sup>6</sup>. Formaldehyde is rapidly distributed to the liver, kidneys, and lungs; to tissues with a high cell turnover (blood-forming organs, lymphoid system, gastrointestinal mucosa); and to tissues with high rates of protein synthesis (exocrine pancreas and salivary glands). Distribution, however, is limited by the high reactivity of formaldehyde which may readily undergo chemical transformation at the site of contact. Indeed, metabolism of formaldehyde may proceed *via* two mechanisms, namely the metabolic and chemical pathways<sup>4</sup>. The metabolic pathway requires enzyme participation and consists in the oxidation of formaldehyde to formic acid and carbon dioxide, and in the incorporation of formaldehyde into biosynthetic pathways leading to protein and nucleic acids. On the other hand, the chemical pathway involves interaction of formaldehyde with nucleophilic amines, sulfur or hydroxyl groups located on

amino acids, nucleotides and other essential cell components which constitute the forming blocks of proteins, RNA, and DNA. DNA-protein cross-links have been detected in tissues exposed directly to formaldehyde, but not in tissues remote from the absorption site.

Formaldehyde is rapidly eliminated from the systemic circulation and tissues through the various transformation pathways discussed above. A substantial amount is also excreted *via* the lung as exhaled CO<sub>2</sub>, while minimal quantities may be found in the urine as adducts<sup>1</sup>. The half-life of formaldehyde was estimated at 100 minutes, with a rate constant of 0.42/h<sup>1</sup>.

## 1.2 Toxicology

The effects of formaldehyde have been extensively studied in both animals and humans as a result of the widespread exposure experienced by individuals to indoor air formaldehyde released from building materials and furnishings.

The most predominant acute effects of formaldehyde exposure reported in humans are various kinds of physical symptoms emanating from the irritation of the mucosa in the eyes and upper airways as well as skin sensitivity. Symptoms displayed by humans after short-term exposure are similar to those observed in animals and include: irritation of the eyes, nose and throat, together with exposure-dependent discomfort, lachrymation, sneezing, coughing, nausea, and dyspnea<sup>6</sup>. Numerous reports also show that exposure to formaldehyde vapours causes direct nonimmunological irritation of the skin, and may also contribute to the development of asthma in a small segment of the population exposed to high concentrations of the chemical. Allergic reactions resulting in respiratory tract, skin, and systemic sensitization have also been reported.

The potential of formaldehyde to produce chronic respiratory tract disease in humans has been reported by several cohort and cross-sectional studies, however, no firm conclusion could be obtained by a detailed examination of the literature performed by a WHO task force<sup>5</sup> in view of the numerous confounding factors present in design protocols, and absence in certain cases of accurate exposure level measurements. Similarly, although both neurochemical and morphological changes have been reported in the nervous system of acutely exposed experimental animals, neuropsychological effects have been difficult to observe in humans chronically exposed to formaldehyde concentrations ranging from 8 ug/m<sup>3</sup> to 430 ug/m<sup>3</sup> (0.007 - 0.35 ppm). Finally, WHO<sup>6</sup> has commented on the potential reproductive and developmental effects of formaldehyde, and concluded that owing to the scarcity and limitations of the available data no definite conclusions could be drawn on the relevance of these effects in humans.

According to both WHO<sup>6</sup> and IARC<sup>5</sup> reports, the evidence for the genotoxicity of formaldehyde in humans is conflictual, although the weight of evidence supports the absence of *in vivo* activity for this chemical<sup>6</sup>. On the other hand, formaldehyde has been reported to be genotoxic in a variety of test systems encompassing a broad range of end-points and levels of phylogenetic complexity<sup>3,5</sup>. It has been shown to be mutagenic in multiple bacterial test systems (with and without metabolic activation), fungi, and *Drosophila*. Formaldehyde also induces SCEs and chromosomal aberrations and causes adduct formation with DNA repair in cultured human cells.

An excess of several forms of cancer has been reported in various epidemiological studies relating to formaldehyde. Neoplastic events have included: Hodgkin's disease, leukemia, cancer of the buccal cavity and pharynx, lung, nose, prostate, bladder, brain, colon, skin, and kidney<sup>5,6</sup>. However, some of these effects have been attributed to secondary factors not related to formaldehyde. On the other hand, it appears that upper respiratory tract cancers may be causally related to formaldehyde in view of the solubility and rapid metabolism of this chemical. IARC<sup>5</sup> has determined that the overall evidence of carcinogenicity of formaldehyde to humans is limited and, consequently, classified formaldehyde in Group

2A. Similarly, formaldehyde was classified in Group B1 by the U.S. EPA<sup>6</sup> based on limited evidence in humans. In both cases it was concluded that the evidence of carcinogenicity in animals was sufficient.

The effects that formaldehyde induces in animals are comparable to those observed in humans, and include skin and mucosa irritation and sensitization. In addition, pathological effects associated with exposure to high concentrations of formaldehyde (in acute, sub-acute, and sub-chronic studies) by the inhalation route have resulted in squamous metaplasia in part of the transitional and respiratory epithelium of the upper and lower respiratory tract; ulceration or necrosis of the nasal turbinate mucosa, tracheal mucosal ulceration and necrosis, and pulmonary congestion, in both rodents and primates. Significant changes in the uterus and ovaries of treated female rats have also been reported. Oral exposure of rats to high concentrations of formaldehyde in drinking water has resulted in similar portal-of-entry effects in the gastrointestinal tract, more specifically in the upper part where hyperkeratosis and gastritis in the fore- and glandular stomach has been reported. These effects in both the upper respiratory and gastrointestinal tracts reflect the high reactivity of formaldehyde which promptly reacts with biological tissue components. This is supported in most reports by the absence of significant systemic effects at distant sites (*e.g.*, liver, kidney).

Exposure of animals to lower concentrations of formaldehyde vapors for longer periods of time (lifetime) resulted in comparable changes in the nasal passages with the addition, in some cases, of neoplastic events. In this case, it is interesting to note that tumors in the upper airways frequently occurred following co-exposure or post-exposure to other compounds such as hydrogen chloride and diethylnitrosamine, respectively. Similarly, lifetime exposure of animals to low concentrations of formaldehyde in drinking water did not result in any neoplastic event. Based on these (and other) observations, some investigators have suggested that formaldehyde may not be a complete carcinogen, and act as a promoter<sup>5</sup>. This controversial issue, which has not been resolved yet, is of importance when assessing potential human health risks to formaldehyde as it determines which conceptual approaches (*i.e.*, threshold *versus* non-threshold) will be the most appropriate. As previously mentioned, for both the U.S. EPA<sup>6</sup> and IARC<sup>7</sup> the evidence of carcinogenicity for formaldehyde in animals is considered sufficient.

## 2. DOSE-RESPONSE INFORMATION/CURRENT EXPOSURE GUIDELINES

The uncertainties surrounding the potential toxicological effects of environmental formaldehyde on communities have influenced significantly the methodologies used to set guidelines and permissible exposure levels. The adoption of reasonably conservative assumptions is warranted in this context in order to provide sufficient protection of public health. This section summarizes various health criteria values, that is, exposure guidelines and dose-response information that leading regulatory agencies (and other relevant sources) have proposed and consider appropriate for permitting, assessing, and characterizing risks associated with various exposures. Potential exposures to formaldehyde are evaluated in section 3 and the risk characterization is presented in section 4.

### 2.1 Air Guidelines

#### 2.1.1 Chronic, Non-Carcinogenic Health Effects

The US EPA's Integrated Risk Information System database<sup>8</sup> notes that the inhalation Reference Concentration (RfC) for formaldehyde is not available at this time. EPA defines an RfC as an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime.



The California Air Pollution Control Officers Association (CAPCOA)<sup>9</sup> has reported for formaldehyde, in January 1992, an inhalation chronic AEL (Acceptable Exposure Level) of 3.6 ug/m<sup>3</sup>. Similarly, the Massachusetts Department of Environmental Protection (MDEP)<sup>10</sup> has proposed a Threshold Effect Exposure Limit (TEL) of 0.33 ug/m<sup>3</sup>. These values, derived based on information from the US EPA and the American Conference of Governmental Industrial Hygienists (ACGIH) TLV in the case of CAPCOA, and of the ACGIH TLV in the case of MDEP, are used for the evaluation of the potential noncancer adverse health effects of long-term (chronic) exposures.

No equivalent exposure limits were available from WHO<sup>6</sup> which advocates a 30 minutes, time-weighted-average (TWA) of 100 ug/m<sup>3</sup>, and by the New York State Department of Health (NYSDOH)<sup>11</sup>, which has proposed a Short-Term Guideline Concentration (SGC) (1 hour) of 30 ug/m<sup>3</sup>. Although explicit rationales were not provided in the referenced documents, these values are purported to prevent short-term, acute effects such as irritation of mucosal membrane. They are not applicable for the evaluation of long-term, non-carcinogenic effects.

Generally, the inhalation chronic AEL, TEL, and the inhalation RfC noted above are comparable in their use for assessing chronic effects (except carcinogenic effects) due to inhalation.

## 2.1.2 Carcinogenic effects

For the purpose of estimating cancer risk, the U.S. EPA<sup>8</sup>, in 1987, has established an inhalation unit risk of  $1.3 \times 10^{-5}$  (ug/m<sup>3</sup>)<sup>-1</sup> for continuous lifetime exposure to 1 ug/m<sup>3</sup> of formaldehyde, based on animal inhalation studies. This correspond to an ambient air level of 0.08 ug/m<sup>3</sup> associated with an excess lifetime cancer risk of 1 in 1,000,000. Due to the chemical reactivity of formaldehyde and to the induction of portal-of-entry effects in both the upper respiratory and gastrointestinal tracts, calculation of an oral slope factor based on the simple conversion of the unit risk factor is not recommended. In fact, the unit risk factor derived by the US EPA is based on the incidence of squamous cell carcinomas in the nasal cavity, an effect that may be considered unique to the inhalation of formaldehyde. It should also be noted that due to the uncertain nature of the mechanisms by which formaldehyde induces cancer, to the equivocal genotoxicity of this compound *in vivo*, and to the presence of an apparent threshold in bioassay results, the non-threshold concept and, hence, the application of the linearized multi-stage model advocated by the US EPA is currently under attack. It is most likely that the current unit risk factor in IRIS<sup>8</sup> should be considered provisional until new and more relevant mechanistic data becomes available.

In fact since 1987 the EPA has obtained data regarding nasal DNA binding of formaldehyde in the form of DNA-protein cross-links (DPX) and, using the quantitation of these DPX levels as an internal measure of formaldehyde dose, developed revised unit risk estimates (US EPA)<sup>7</sup> which are somewhat less conservative. The EPA believes that the use of DPX data as a surrogate for dose is appropriate with the following reservations: a) the DPX data were obtained following an acute exposure to formaldehyde whereas the rat study was a chronic two year study, b) the role of DPX, if any, is not completely understood (i.e. it could have a mechanistic role), and c) there may be species differences in sensitivity. EPA favours the risk estimate based on monkey data (ie.  $6 \times 10^{-7}$ ; see Table A) because the monkey may be a closer surrogate to humans than the rat, and the epidemiological data indicates the whole nasal region as the most likely possible target for formaldehyde-induced cancer (tumours in the rat are most prevalent in the anterior portion of the nasal cavity).

As noted below both the New York State Department of Health (NYSDOH), and the California Air Resources Board (CARB) have developed unit risk estimates using the Kerns et. al.<sup>30</sup> study together with DPX data but using different assumptions regarding estimation of dose and scaling factors. All the formaldehyde unit risk estimates are summarized in Table A.



The New Jersey Department of Environmental Protection and Energy<sup>12</sup>, the Massachusetts Department of Environmental Protection, and the states of Florida, Indiana, and Kansas<sup>14</sup>, all have adopted the US EPA unit risk of  $1.3 \times 10^{-5} \text{ (ug/m}^3\text{)}^{-1}$ . No oral potency factor has been recommended by these jurisdictions. A comparable value of  $1.7 \times 10^{-5} \text{ (ug/m}^3\text{)}^{-1}$  was developed and recommended recently by the New York State Department of Health (NYSDOH), as reported in their recent New York State Air Guide-1<sup>11</sup>, thus resulting in an Annual Guideline Concentration (AGC) of  $6 \times 10^{-2} \text{ ug/m}^3$  for an excess cancer risk of  $10^{-6}$ . Similarly, the current Allowable Ambient Limit (AAL) for the State of Massachusetts is  $8 \times 10^{-2} \text{ ug/m}^3$ . Several other US states may have adopted the US EPA methodology. However, different averaging times, widely varying values for similar averaging times, and other considerations that may be related to risk management policies make comparison of air guidelines difficult<sup>14</sup>. Values generally range from 0.08 to  $8 \text{ ug/m}^3$ .

More recently, the California Air Resources Board (CARB) has reviewed and reassessed the evidence available on the carcinogenicity of formaldehyde<sup>13</sup>. Based on the same animal database as that used by the US EPA, CARB recommended a unit risk factor of  $6 \times 10^{-6} \text{ (ug/m}^3\text{)}^{-1}$ . Major changes in methodologies included the use by CARB of the rate of binding of formaldehyde to DNA in the nasal lining of the rat, and three different scaling factors to extrapolate the equivalent dose rate from rats to humans.

Table A. Comparison of Formaldehyde Unit Risk Estimates

Source	Classification	Unit Risk Estimate ( $\text{ug/m}^3$ ) <sup>-1</sup> Upper Bound	Air Concentration ( $\text{ug/m}^3$ ) for Specific Risk Level		
			$10^{-4}$	$10^{-5}$	$10^{-6}$
EPA (1987)	Group B1, probable human carcinogen	$1.3 \times 10^{-5}$	8.0	0.8	0.08
EPA (1991)	Group B1	$6 \times 10^{-7a}$	167	16.7	1.67
		$8 \times 10^{-6b}$	125	12.5	1.25
CARB (1992)	Probable Human Carcinogen	$6 \times 10^{-6}$	17	1.7	0.17
NYSDOH (1991)		$1.7 \times 10^{-5}$	6	0.6	0.06

<sup>a</sup> Calculated using monkey DPX data

<sup>b</sup> Calculated using rat DPX data

No unit risk factor and air guidelines for formaldehyde have been recommended by the International Agency for Research on Cancer<sup>15</sup>, and by the World Health Organization, Regional Office for Europe<sup>6</sup>, respectively, in view of the uncertainties surrounding the evidence of genotoxicity, human carcinogenicity, and potential presence of a threshold in the bioassay dose-response data.

The current Ambient Air Quality Criterion (AAQC; with an averaging time of 1 hour) and the half-hour Point of Impingement ( $\frac{1}{2}$ h POI) value in Ontario is, for both cases,  $65 \text{ ug/m}^3$ . This value was developed in 1974 and is based on odour. Both these values are currently under review/update by the Ministry.

Occupational exposure guidelines have been developed for formaldehyde. In the U.S., the Permissible Exposure Limit (PEL), established by the Occupational Safety and Health Administration (OSHA)<sup>17</sup> is 0.75

ppm (925  $\mu\text{g}/\text{m}^3$ ). The American Conference of Industrial Hygienists (ACGIH)<sup>17</sup> presently has a Threshold Limit Value-Time Weighted Average (TLV-TWA) of 0.3 ppm (370  $\mu\text{g}/\text{m}^3$ ) with a notification A2(i.e., suspected human carcinogen).

The current Ontario occupational guideline for formaldehyde is 1500  $\mu\text{g}/\text{m}^3$  (1 ppm) with a Short-Term Exposure Value (STEV) of 3000  $\mu\text{g}/\text{m}^3$  (2 ppm). A new value, 180  $\mu\text{g}/\text{m}^3$  (0.03 ppm) was recently proposed<sup>18</sup> based on a recent review of five jurisdictions, with the most stringent value having been selected.

A Federal-Provincial Advisory Committee on Environmental and Occupational Health developed in 1987, exposure guidelines for residential indoor air quality<sup>31</sup>. For formaldehyde an action level of 120  $\mu\text{g}/\text{m}^3$  and a target level of 60  $\mu\text{g}/\text{m}^3$  was recommended. The committee recommended that because of the possible carcinogenicity of formaldehyde, it would be prudent to reduce indoor levels as much as possible. The action level of 120  $\mu\text{g}/\text{m}^3$  was the lowest concentration considered to be feasible at that time. However, it was recommended that in future, and where remedial measures are taken, every effort be made to reduce concentrations to below the target value (60  $\mu\text{g}/\text{m}^3$ ).

The above guidelines for atmospheric formaldehyde are summarized in Table 1 below.

## 2.2 Other Route Guidelines

There appears to be no human studies regarding cancer effects after oral exposure to formaldehyde. No strong evidence of neoplastic events have been reported in rodents fed formaldehyde alone for a lifetime, although lesions considered to be early precursor of the evolutionary carcinogenic response (e.g., squamous cell hyperplasia, basal cell hyperplasia, etc.) have been repeatedly observed in the upper digestive tract<sup>1</sup>. As a result, no oral potency factor is currently available for formaldehyde<sup>8</sup>.

The US EPA has proposed a Reference Dose (RfD) of 0.2 mg/kg-day set to prevent systemic, non-carcinogenic effects. The RfD, developed from a lifetime bioassay in rats (drinking water), was based on a NOAEL of 15 mg/kg-day for reduced weight gain and histopathology. Once again, however, portal-of-entry effects in the upper part of the digestive tract prevent the utilization of the oral RfD for calculating an inhalation RfC.

No other regulatory agencies or US state jurisdictions appear to have proposed either an oral potency factor or an RfD to this date. No drinking water health advisories for the purpose of assessing short-term exposures have been issued by the US EPA<sup>8</sup>. Similarly, no water quality guidelines, and more specifically Maximum Allowable Concentration (MAC) are available in Canada, although a value is presently in preparation.

The above ingestion guidelines are summarized in Table 1.

TABLE 1. Summary of Exposure Guidelines for Formaldehyde from Leading Agencies

GUIDELINE APPLICATION	AGENCY(IES) (4)	ORIGINAL VALUE	CONCENTRATION ("Original Form" converted to these as applicable)			CALCULATED "ALLOWABLE" INTAKE (3)
			Unit Risk(1)	RsC (2) (1 x 10 <sup>-4</sup> )	RsC (2) (1 x 10 <sup>-4</sup> )	
INHALATION GUIDELINES						
Occupational	OSHA, ACGIH, OMOL	370 - 1500 ug/m <sup>3</sup>	NA	NA	NA	7400 - 30000 (0.11 - 0.43)
Ambient Air Quality Guidelines	US states,	0.08 - 8 ug/m <sup>3</sup>	NA	NA	NA	1.6 - 160 (2.3 x 10 <sup>-5</sup> - 2.3 x 10 <sup>-3</sup> )
Ontario Air Quality Guideline	MOEE	65 ug/m <sup>3</sup> (1h)	NA	NA	NA	Not applicable since MOEE value is odour based.
Indoor air guideline	H&W Canada	60 ug/m <sup>3</sup>	NA	NA	NA	1200
Chronic AELs/RfCs	CAPCOA, MDEP	0.33 - 3.6 ug/m <sup>3</sup>	NA	NA	NA	6.6 - 72 (9.4 x 10 <sup>-5</sup> - 1 x 10 <sup>-3</sup> )
Inhalation Cancer Potency Factor	US EPA(1987) US EPA (1991) NYSDOH CARB	See Unit Risk column	1.3 x 10 <sup>-4</sup> 6.0 x 10 <sup>-7</sup> 1.7 x 10 <sup>-4</sup> 6 x 10 <sup>-6</sup>	0.8 16.7 0.6 1.7	0.08 1.7 0.06 0.17	for 1 x 10 <sup>-5</sup> risk: 12 - 334 (1.7 x 10 <sup>-4</sup> - 4.8 x 10 <sup>-3</sup> ) for 1 x 10 <sup>-6</sup> risk: 12 - 33 (1.7 x 10 <sup>-5</sup> - 5 x 10 <sup>-4</sup> )
INGESTION GUIDELINES						
Oral Reference Dose (RfD)	US EPA	0.2 mg/kg-day	-	-	-	14000 (0.2 mg/kg-day; oral route)
Drinking Water Guideline	NA	-	-	-	-	-
Oral Cancer Potency Factor	NA	-	-	-	-	-

See next page for footnotes.

### Footnotes to Table 1.

- 1) For inhalation and ingestion guidelines, unit risks are expressed as  $(\mu\text{g}/\text{m}^3)^{-1}$  and  $(\mu\text{g}/\text{L})^{-1}$ , respectively
- 2) For inhalation and ingestion guidelines, risk specific concentrations are expressed as  $\mu\text{g}/\text{m}^3$  and  $\mu\text{g}/\text{L}$ , respectively
- 3) Intake was computed by assuming, where applicable, an adult weight of 70 kg, a breathing rate of 20  $\text{m}^3/\text{day}$ , a water intake of 1.5 L/day. In all cases 100% bioavailability of the intake was assumed.
- 4) See glossary for agency definitions.

## 3. HUMAN EXPOSURE ASSESSMENT

### 3.1 Inhalation

#### 3.1.1 Ambient Air Quality

Ambient levels of formaldehyde have been measured at two fixed site stations in Windsor by the Environmental Protection Service of Environment Canada. The measurement period extends from 1989 to 1992 and includes 146 samples of 24 hour average each. In addition, during the summer of 1991 and the winter of 1992, 49 samples of 24 hour average each, have been collected outside the homes of several Windsor volunteers. The monitoring methodology used for these two sets of samples were the same. The two data sets were combined (ie. a total of 195 samples) to give a more representative data set for outdoor air in Windsor. Concentration levels range from non-detectable to 25.1  $\mu\text{g}/\text{m}^3$ , with the median, mean (average), 90th percentile and 95th percentile levels being 2.67, 3.60, 7.60 and 8.87  $\mu\text{g}/\text{m}^3$ , respectively<sup>16</sup>.

It is possible to estimate the daily intake of formaldehyde associated with these measures of Windsor ambient air quality, recognizing that personal real exposures/intakes may be quite different as further discussed in section 3.1.2. Table 2 below shows these estimated intakes for two different receptors, i.e., an adult and a child. It should be noted that these intakes were calculated based on 24 hour exposures and assume 100% bioavailability by the inhalation route.

**Table 2. Estimated Daily Intakes of Formaldehyde Associated With Ambient Air Quality in Windsor**

Air Quality Measure(a)	Concentration	Adult(b)	Child(b)
	$\mu\text{g}/\text{m}^3$	$\mu\text{g}/\text{day}$ ( $\mu\text{g}/\text{kg}\cdot\text{day}$ )	$\mu\text{g}/\text{day}$ ( $\mu\text{g}/\text{kg}\cdot\text{day}$ )
Median	2.67	53.4 (0.76)	13.4 (0.89)
Mean	3.60	72.0 (1.03)	18.0 (1.2)
90th percentile	7.60	152 (2.17)	38 (2.53)
a) Based on 195, 24 hour average samples b) Assuming the following weights and inhalation rates per day (ie. per 24 hour period): Adult: 70 kg; 20 $\text{m}^3/\text{day}$ Child: 15 kg; 5 $\text{m}^3/\text{day}$			



### 3.1.2 Microenvironments

It is reasonable to assume that the daily formaldehyde intakes associated with typical personal exposure patterns can be better estimated from various microenvironmental concentrations than from fixed site monitoring data. For the purpose of scoping population exposures, the set of typical receptors in Table 3 below was considered. Examples of the receptor types and/or their characteristics are also included in Table 3. Using formaldehyde concentrations acquired in various microenvironments, either as part of the personal exposure or subsequent microenvironment study in Windsor, it is possible to scope out various typical personal inhalation exposure scenarios for the above receptors. The estimated daily intakes (in ug/day) of these receptors are summarized in Table 4.

Table 3. Receptors With Typical Personal Exposure Patterns

NAME OF RECEPTOR TYPE	CHARACTERISTICS	NAME OF RECEPTOR TYPE	CHARACTERISTICS
Average Office Worker (Non-smoking)	Eg. - Typical office worker (Based on Windsor volunteers and US EPA TEAM study; not smoking at home)	High Outdoor Receptor	Eg. - Construction workers; - Bicycle couriers - Police - Long distance runners
Average Office Worker (Smoker Environment)	Eg. - Typical office worker (Based on Windsor volunteers and US EPA TEAM study; smoking at home)	High Indoor Receptor	Eg. - 'Shut-ins'- Invalids - Elderly, non-mobile
Average Youth	Eg. Special exposures at shopping malls and athletic facilities (pools) in addition to school;	High Commuting Receptor	Eg.- Bus drivers - Taxi drivers - Delivery/ Distribution Services
Average Child (Non-Smoker Home & No Exposure to Tobacco Smoke)	Eg. Similar to average office worker except 'School' replaces 'Office';	Active Receptor # 1	Eg.- 7 hr/week in Bingo Hall or Bar
Average Child (Non-Smoker Home & Typical Exposure to Tobacco Smoke)	Eg. Includes typical times that children may be in proximity to tobacco smoke, outside the home, based on activity pattern studies;		
Average Child (Smoker Home with Exposure to Tobacco Smoke)	Eg. Child living in a house where there is a smoker		

A microenvironment, in which measurements were not taken, but which may be a source of formaldehyde exposure, common to all the above receptors, is the bathroom during bathing and showering. However, in light of the uncertainties on actual concentrations in Windsor drinking water (see s 3.2.2), it is not reasonable to calculate the inhalation exposure for this scenario.



Table 4. Estimated Daily Intakes (ug/day) Associated with Typical Personal Exposures (See footnote 1,1)

MICRO ENVIRONMENT	Air Concentration (ug/m <sup>3</sup> ) (h)	Average Office Worker Non-smoker	Average Office Worker Smoker Environment	Youth	Average Child Non smoker home/No exposure to tobacco smoke	Average Child Non smoker home/Typical exposure to tobacco smoke	High Outdoor Receptor	High Indoor Receptor	High Commuting Receptor
Office	17.6/39.9 (m)	6.7(a)	6.7(a)				1.7		
School	17.6/39.9 (d)			6.7	6.7	6.7			
Home	27.1/45.7 (m)	13.3(b)		13.3	13.7	12.4	13.7	20.4	13.7
Commuting (in-transit)	15.4/35.4 (o)	1.0(a)	1.0(a)	1.0(f)	1.0(f)	1.0(f)	1(a)	1(a)	7.7
Urban (Outdoors)	3.6/ 7.6	2.6(a)	2.6(a)	2.6	2.6	2.6	7.6(g)	2.6	2.6
Home with smokers	39.4/31.8 (c)		13.7(b)			1.3(e)			
Shopping Mall/Market	17.6/39.9 (m)	0.4(i)		0.4(i)					
Bar or Bingo Hall	76.3/89.7 (k)								
INTEGRATED EXPOSURE (ug-hrs/m <sup>3</sup> )		510.2/ 946.3	682.5/ 1234.9	510.2/ 946.3	514.0/ 948.6	529.9/ 975.8	444.0/ 787.1	577.6/ 987.4	499.2/ 918.4

TIME WEIGHTED AVERAGE EXPOSURE (ug/m <sup>3</sup> over 24 hr) (h)	22.3/39.4	28.4/51.5	21.3/39.4	21.4/39.5	22.1/40.7	18.5/32.8	24.1/41.1	20.8/38.3
INTAKE/DAY (UG/DAY) (h)	425.1/788.6	568.7/1029.1	297.6/ 552.0	107.1/197.6	110.4/203.3	370.0/ 656.0	481.3/ 822.9	416.0/765.4

### Estimations:

- \*  $\text{INTEGRATED EXPOSURE (ug-hrs/m}^3\text{)} = \text{SUM OF [Microenvironment concentration} \times \text{Time spent in Microenvironment]}$
- \*  $\text{TIME WEIGHTED AVERAGE EXPOSURE (ug/m}^3\text{)} = \text{INTEGRATED EXPOSURE/24 hr}$
- \*  $\text{INTAKE/DAY (ug/day)} = \text{TIME WEIGHTED AVERAGE EXPOSURE} \times \text{DAILY BREATHING RATE (ie. for Adult or Youth or Child as applicable)}$

### Footnotes:

- a.) TIME BUDGET ANALYSIS; Windsor '91 Summer PEP Study; Handout to Volunteers; May/92 (R. Bell)
- b.) Sum of 'Indoor, Home' and 'Indoor Other' in a.)
- c.) This value was obtained during the personal exposure study in Windsor from homes where smoking was permitted.
- d.) Assumed to be same 'microenvironment' concentration that were measured by PEP study in the 'Office' environment.
- e.) Average time spent in proximity to tobacco smoke, in various locations outside the home, was approximately 1.3 hours, based on a study of children's activity patterns; (Ref: Study of Children's Activity Patterns, State of California, Air Resources Board, Contract No. A 733-149). Assume that benzene concentrations, when in proximity to tobacco smoke is represented by the median levels referenced in footnote "c," above.
- f.) Assume 1 hour is spent in the car per day.
- g.) For the 'high-outdoor' receptor, urban outdoor concentrations were assumed to be represented by the 'mean' and 90th percentile concentrations taken from the fixed site monitoring network. Also assume that for this group, the 6.7 hours of 'at work' exposure is divided so that 1.7 hours is spent in the office and 5 hours is added to the 2.6 hours of urban outdoor exposure for a total of 7.6 hours.
- h.) First number is the 'mean'. The second number is the 90th percentile, if available; otherwise, it is the maximum value measured.
- i.) Assumed that approximately 2.8 hours per week are spent on malls shopping; this was distributed over seven days yielding '0.4 hours/day' on malls.
- j.) Assumed that this receptor spends approximately 7 hours per week in a bingo hall or bar; this was distributed over seven days yielding '1 hr/day' in bingo halls or bars.
- k.) The average and maximum values of the 'bingo hall' (ie. 76.3 ug/m<sup>3</sup>) microenvironment were used to represent both of these microenvironments.
- l.) Two additional typical personal exposure patterns that were evaluated but are not shown in detail in this table are the 'Average Child in a Smoker Home' and the 'Active Receptor # 1' as noted in Table 3 above. The corresponding intakes/day (ie. mean/90th percentile) for these two receptors are 142.2/257.3 and 469.3/827.2, respectively.
- m.) The 'mean' and '90th percentile' concentrations for the 'Office', 'Home' and 'Commuting' microenvironments were derived from the Summer 1991 and Winter 1992 personal exposure studies in Windsor.
- n.) Formaldehyde was not measured at the 'market' microenvironment. It was assumed that the 'Sh. mall/Market' microenvironment can be represented by the same concentration as that of the 'Office' microenvironment.
- o.) Formaldehyde was not measured in the 'commuting' microenvironment in the Windsor study. The mean and maximum values were adopted from an in-vehicle air toxic characterization study (Ref: 'Motor Vehicle Related Air Toxics', EPA 420-R-93-005; US EPA, April 1993, pp 6-22).

In order to place the above inhalation exposures (ie. intakes) in Windsor in perspective, it is appropriate to compare to daily intakes that people who smoke may experience.

### 3.1.3 Smoking.

Formaldehyde has been detected in cigarette smoke and exposure occurs both through direct inhalation by smokers and from side stream smoke. The average yield for mainstream smoke is 70-100 ug/cigarette for non-filter cigarettes (Reference 27, Table 3.2, p.53). The yield for sidestream smoke from filter cigarettes is 700 ug/cig (Reference 27, Table 3.5, p.56). For the Kentucky reference 1R4F filter cigarette, the mainstream yield is 20 ug and the sidestream is 730. The authors note that filters and changes in tobacco processing have reduced mainstream deliveries considerably whereas sidestream deliveries have remained fairly constant.

Because formaldehyde is a relatively reactive species and because other sources, such as consumer products and building materials, also emit it, it is difficult to demonstrate a definite contribution from smoking to indoor concentrations of formaldehyde (Reference 27, Table 10.2 and 10.3, p.204; p.207). A person who smokes a pack a day (25 cigarettes) would therefore inhale between 500 and 2500 ug/d. The lower bound would apply to filter cigarettes. Much of it is likely to be absorbed through the mucosal membranes of the nose and upper respiratory tract (s.1.1).

Non-smokers who are heavily exposed to environmental tobacco smoke inhale the equivalent of 1/3 to 3 cigarettes per day or 7 to 300 ug of formaldehyde/day (Blot and Fraumeni<sup>23</sup>). Vainio<sup>26</sup> states that the exposure of non-smokers to environmental tobacco smoke would be about 1% of that of active smokers or 5 to 25 ug/day, whereas Remmer<sup>25</sup> gives as an upper limit the equivalent of only 1/5 of a cigarette per day or about 4 to 20 ug/day. Hiller<sup>24</sup>, quoting other authors, gives intakes ranging from a low of 0.001 cigarette equivalents (CE)/hr or 0.01 CE/day, assuming 12 hr exposure, to a high of 27 CE/day. The higher value is clearly anomalous as the range claimed by the other authors is 0.001 to 0.2 CE/hr. The lower value gives an intake of 0.2 to 1 ug/day. Because of the reactivity of formaldehyde, which rapidly reduces its concentration in air, the lower end of the range is more likely; that is, somewhere around 5 ug/d.

Furthermore, it is also important to place the inhalation exposures (ie. intakes) in Windsor into perspective, relative to general exposures from other media (ie. see Section 3.2).

## 3.2 Other Routes

In this section, possible non-inhalation routes of exposure (ie. ingestion and dermal) are assessed.

### 3.2.1 Ingestion of Food

There is no data on the content of formaldehyde in foods eaten by Windsor residents. However, the chemical has been quantified in foods. According to the studies cited by the World Health Organization (Reference 1, p.49 and 67) the concentrations in food range from 1 to 100 ug/g, with most food types containing <15 ug/g. The content is quite variable. Depending on the diet, the daily intake for an adult is estimated to range between 1.5 and 14 mg. The amount of food consumed by a child (<11 years) is ≈ 70% that of an adult. Assuming a similar diet for children the estimated intakes range between 1 and 10 mg. Most of the chemical is stated to be in *bound and unavailable form*. The source of the formaldehyde may be natural, but it can be introduced through cooking and especially smoking of food. In addition, it can be eluted from formaldehyde-resin dishes, such as melamine, by water and vinegar according to a 1975 study. WHO, in a different publication, gives a range of 1.7-14.2 mg/d<sup>6</sup>. The same



studies are cited in a report by EPA (Reference 21, p.19). It should be noted that all the cited analyses are from 1982 and earlier.

### 3.2.2 Drinking Water

There are no data available on the concentrations of formaldehyde in the Windsor drinking water supply. The Drinking Water Section, Water Resources Branch of MOEE reports that no method exists at present for the routine analysis of formaldehyde in drinking water. However, it has not shown up in any mass spectrometer scan. Further, formaldehyde in drinking water is believed to be a byproduct of ozonation, a process confined at present to Kitchener and Atikokan.

According to WHO<sup>1</sup> (p.67), the concentrations in drinking water are normally  $<0.1$  mg/L, leading to an intake of  $<0.2$  mg/d for an adult or child. Average concentrations measured in rainwater in the mid 1970s range from 0.11 to 0.17 mg/L. This would be a maximum estimate. Since it has not been detected in Ontario water supplies, the intake would be much less. Absorption of formaldehyde from the gastrointestinal tract occurs quite rapidly and blood levels of the compound following oral ingestion are similar to blood levels following inhalation of the compound (Reference 21, p. 27). This suggests that the absorption of formaldehyde from drinking water is high, possibly 100 %.

Although volatilization from water is not expected under normal environmental conditions because of the high water solubility, formaldehyde in water is rapidly (in days) biodegraded by several species of microorganisms, provided the concentration is not too high. The low octanol/water partition coefficient suggests that adsorption on suspended solids and partitioning to sediments is not significant (Reference 1, p.12; Reference 21, p.8).

### 3.2.3 Soil

There is no information on the levels of formaldehyde in the soil in the Windsor study area. It is formed in the early stages of the decomposition of plant residues in soil, but soil bacteria degrade it so that there is no bioaccumulation (Reference 1, p.48).

The high water solubility and low  $K_{ow}$  of the chemical suggest that soil adsorption will be low. The calculated  $K_{oc}$  of  $\approx 5$  suggests that formaldehyde is very mobile in the soil and easily leached. Since it is a gas at room temperature, it can be expected to evaporate from soil (Reference 21, p.16).

It is unlikely, therefore, that the ingestion of soil will prove to be a significant exposure pathway for formaldehyde.

### 3.2.4 Dermal

Dermal exposure and adsorption can occur through contact with cosmetics, household products, disinfectants and textiles. Such exposures are localized and the amount absorbed is estimated to be negligible (Reference 1, p.68). Absorption is likely to be significant only if the pure compound is applied to the skin. Although absorption of pure formaldehyde has been reported to be 55-60% irrespective of dose in rats and guinea pigs, it is  $<1\%$  in monkeys (Reference 21, p.26). Experiments using aqueous solutions and ointments containing formaldehyde showed that, both *in vivo* and *in vitro*, the maximum amount absorbed over 48 hr was  $\approx 2.5\%$  of the applied dose. On the other hand,  $16.7 \text{ ug/cm}^2\text{-hr}$  was absorbed from a solution of 10% formalin in phosphate buffer in an *in vitro* experiment using human skin



(Reference 1, p.78). Formaldehyde absorbed through the skin enters the bloodstream and is biologically available to the body.

### 3.2.4.1 During Showering and Bathing

EPA (Reference 22, p. 5-49 *et seq*) has proposed a model for transient state dermal adsorption from water. The basic formula for organic compounds is, for  $t_{\text{event}} < t^*$

$$DA_{\text{event}} = 2K_p C_v (6\tau t_{\text{event}} / \pi)^{1/2}$$

where:  $DA_{\text{event}}$  is dose absorbed per unit area per event ( $\text{mg}/\text{cm}^2 \cdot \text{event}$ )

$K_p$  is the permeability coefficient ( $\text{cm}/\text{hr}$ )

$C_v$  is the concentration in the water ( $\text{mg}/\text{cm}^3$ )

$t_{\text{event}}$  is the time spent showering or bathing ( $\text{hr}$ )

$\tau$  is a number calculated from the skin thickness and diffusivity of the chemical in the skin ( $\text{hr}$ )

$t^*$  is number that is calculated from the value of  $B$  ( $\text{hr}$ ) ( $B = K_{ow}/10^4$ ;  $K_{ow}$  is the octanol/water partition coefficient)

Table 5-8 in US-EPA (1992) gives the appropriate values to use in the above equation. For formaldehyde, the estimated value for  $K_p$  is  $0.0022 \text{ cm}/\text{hr}$ , for  $\tau$  is  $0.13 \text{ hr}$  and for  $t^*$  is  $0.32 \text{ hr}$ . Assuming that a shower takes  $0.25 \text{ hr}/\text{d}$ , a median skin surface area of  $19400 \text{ cm}^2$  (table 8-3) for an adult and a water concentration of  $<0.1 \text{ mg}/\text{L}$  (s. 3.2.2), the amount absorbed during a shower is  $<2 \text{ ug}$  for an adult. The amount absorbed by a child is  $<0.8 \text{ ug}$  since its surface area is  $7310 \text{ cm}^2$ .

### 3.2.4.2 Contact With Soil and Dirt

Since there are no data on the concentration of formaldehyde in soil, it is not possible to calculate the dermal absorption from soil and dirt. However, as noted in s. 3.2.3, it is unlikely that the concentration will be high. Therefore, this exposure route is most probably insignificant.

### 3.2.4.3 From Formaldehyde Vapour in the Air

EPA <sup>22</sup> does not provide any permeability constants for the absorption of formaldehyde from air.

## 4. RISK CHARACTERIZATION AND PERSPECTIVES

Exposures, expressed as daily intakes in units of  $\text{ug}/\text{day}$ , were assessed in section 3. Inhalation, ingestion and dermal routes of exposure were considered. Table 5 below summarizes the daily intakes (or ranges of daily intakes), for adults and children, estimated in section 3. It should be noted that in section 3, the intakes for inhalation and sometimes for ingestion assumed 100% bioavailability. The intake for dermal

exposures are amounts absorbed systemically and hence already include bioavailability considerations. Table 5 has two columns for both adults and children. The first set of columns (ie. '100 % Bioav') give the intakes with 100 % bioavailability having been assumed; the second set (ie. 'Bioav. Incl. '), gives intakes for which bioavailability has been taken into consideration (ie. if information was available as noted in the footnotes). This second set of columns should give a better picture of the relative importance of various exposure routes. As far as comparison to exposure guidelines and intakes associated with cancer risk, the intakes in the first set of columns of Table 5 will be used since the exposure guidelines are also expressed as intakes for which we have assumed 100 % bioavailability.

To characterize risks, the various exposure guidelines discussed in Section 2 are compared to the estimated exposures from inhalation and other routes as discussed in Section 3. Because of the assumptions, uncertainties and ranges of values available from both exposures (see Table 5) and the various exposure guidelines (see Table 1), risk characterization is most appropriately done by comparison of ranges of values.

Table 6 below provides a graphic representation of this comparison of exposures, exposure guidelines and intakes associated with inhalation cancer risk based on ug of formaldehyde intake/day (ie. 'INTAKE in Micrograms per day' increasing upwards on the vertical scale).

The middle section of Table 6, "Exposures", depicts the exposures calculated in Section 3, expressed as intake/day (ie. ug/day). The exposures depicted are: *Outdoor Air Quality* - the exposure from spending 100 % of the day outdoors; *Typical Outdoor Exposure* - the exposure from three hours only outdoors, provided for perspective on the contribution to risk solely from contaminants present in outdoor air; *Typical Personal Exposures* - the range of exposures associated with ten different exposure scenarios, combining periods of indoor, outdoor and various microenvironment exposures. Exposure scenarios are included for adults and children, assuming 20 and 5 m<sup>3</sup>/day inhalation rates respectively. For 'outdoor air quality' (ie. 100% outdoor exposure), for 'typical outdoor exposures' (ie. 3 hr), and for the 'typical activity patterns' the ranges shown, bracket the lowest mean to the highest 90th percentile. For perspective purposes, the exposures of smokers directly from smoking activity is also depicted in this section.

The left section of Table 6, "Exposure Guidelines", expresses the various guidelines discussed in Section 2 in terms of calculated "allowable" intake/day for adults and children. The values are taken from Table 1. Within each type of guideline group (eg. outdoor air) ranges of exposure guidelines, when available, are indicated. Thus, ranges of Air Quality Guidelines (ie. 'Outdoor Air'), Occupational guidelines (ie. 'Workplace Air'), a residential indoor air (ie. 'Indoor Air') guideline and chronic health effects based reference concentrations (ie. 'Chronic AEL') are shown. Comparison of "Exposure Guidelines" to "Exposures" should be done with care. For example, occupational guidelines are included for perspective purposes only. For caveats regarding this comparison see section 4.1.1 of the main report.

The right section of Table 6, "Intakes Associated With Cancer Risk", shows the intakes associated with different levels of cancer risk. Ranges of carcinogenic risk levels (associated with  $1 \times 10^{-5}$  risk and  $1 \times 10^{-6}$  risk) are depicted. Comparison of "Exposures" to "Intakes Associated With Cancer Risk" is appropriate for adult exposures only, since cancer risk estimates apply to a lifetime of exposure and people are adults for the majority of their lives. Adult exposures in the bars of the "Exposure" section fall in the top 70 % of the bars which represent exposures of adults and children.

Based on the tabular analysis (Table 5) and the graphic risk characterization (Table 6), the following observations and deductions can be made:

## Health messages:

1) It is apparent, that the ingestion route exceeds all other exposure routes for formaldehyde. Exposures by inhalation are significant but are considerably less. Dermal exposure appears to be least important although due to data limitations this route could not be evaluated.

2) All the inhalation exposures associated with 'outdoor air quality' (ie. 100 % outdoor exposure) and 'personal activity patterns' overlap with or exceed the range of chronic acceptable exposure levels (ie. 6.6 - 72 ug/day from Table 1;) proposed by California (CDHS/CAPCOA) and Massachusetts (MDEP). Exposures associated with typical outdoor exposures (ie. 3 hr) overlaps with the low range of these chronic acceptable exposure levels. These chronic acceptable exposure levels are considered to be purely health based and are protective against all chronic health effects other than cancer risk. Therefore, there is a possibility of long-term health effects associated with all the inhalation exposures.

This comparison of exposures to chronic acceptable exposure levels can also be expressed more quantitatively in the form of a hazard index. These hazard index comparisons for all substances are summarized and are found in section 4.1.5 of the main report.

3) The most conservative range of available exposure guidelines are depicted in Figure 6 under Intakes Associated with Cancer Risk. These guidelines were proposed by CDHS, the US EPA, and the New York State Department of Health (NYSDOH). As shown in Table 6, they overlap with or are exceeded by the estimated exposures. Because people are adults for the majority of their lives, these intakes associated with cancer risk are depicted for adults only. The inhalation intakes for adults associated with 'outdoor air quality' (ie. 100 % outdoor exposure), 'typical outdoor exposure' (ie. 3 hr) and 'typical personal exposures' range between 72 - 152 ug/day, 9 - 19 ug/day and 370 - 1029 ug/day, respectively (from Tables 2, 4 and 5). These intakes and the corresponding doses in mg/kg-day are summarized in Table 7. Using the various potencies from the three agencies, the range of risks associated with 'outdoor air quality' (ie. 100% outdoor exposure) is between  $2.1 \times 10^{-6}$  and  $1.3 \times 10^{-4}$ . Similarly the range of risks associated with 'typical outdoor exposures' (ie. 3 hr) is between  $2.7 \times 10^{-7}$  and  $1.6 \times 10^{-5}$ . Similarly the range of risks associated with 'typical personal exposures' is between  $1.1 \times 10^{-5}$  and  $9.0 \times 10^{-4}$ . The risks associated with 'typical personal exposures' are slightly higher than the risks associated with 'outdoor air quality' which in turn is higher than 'typical outdoor exposures'. This range of risk analysis is summarized in Table 7.

*In view of the most recent 1991 information from the US EPA (ie. section 2.1.2, Table A), the range of risks in Table 7, corresponding to 'EPA ('91)' is considered to be the best range of risk estimates for formaldehyde. Thus, from Table 7, the range of risks associated with 'outdoor air quality' (ie. 100% outdoor exposure) is between  $2.1 \times 10^{-6}$  and  $4.6 \times 10^{-6}$ . Similarly the range of risks associated with 'typical outdoor exposures' (ie. 3 hr) is between  $2.7 \times 10^{-7}$  and  $5.7 \times 10^{-7}$ . Similarly the range of risks associated with 'typical personal exposures' is between  $1.1 \times 10^{-5}$  and  $3.1 \times 10^{-5}$ . The risks associated with 'typical personal exposures' are slightly higher than the risks associated with 'outdoor air quality' which in turn is higher than 'typical outdoor exposures'.*

It should be further noted, that this risk characterization (ie. using carcinogenic risk based limits) is based on an assumed lifetime exposure (i.e. 70 years, every day, for 24 hours) and hence is a very conservative assumption.

4) The exposure that a smoker experiences overlaps with and exceeds the exposures associated with the Personal Activity Patterns and substantially exceeds exposures associated with 'outdoor air quality' and 'typical outdoor exposures'.



**Table 5. Summary of Estimated Daily Intakes and/or Range of Intakes (in ug /day), from Various Exposure Pathways (ie. intakes, assuming 100 % bioavailability and intakes with bioavailability taken into consideration)**

EXPOSURE PATHWAY		ADULT ug/day (100 % Bioav.)	ADULT ug/day (Bioav. Incl.)	CHILD ug/day (100 % Bioav.)	CHILD ug/day (Bioav. Incl.)
INHALATION	Outdoor Air Quality - Windsor (ie. 100 % outdoor exposure)(a)	72 - 152	72 - 152 (h)	18 - 38	18 - 38 (h)
	Typical outdoor exposure (ie. = 3hr)(b)	9 - 19	9 - 19 (h)	2.3 - 4.8	2.3 - 4.8 (h)
	Typical personal exposures(ie. Table 4) (c)	370 - 1029	370 - 1029 (h)	107 - 257	107 - 257 (h)
	Smoking (g)	500 - 2500	500 - 2500(h)		
INGESTION	Food (d)	1500 - 14000		1000 - 10000	
	Drinking water (i)	<<200	<<200		
	Soil (e)	-	-	-	-
	TOTAL (Ingestion)	<1700 - 14000		1000 - 10000	
DERMAL	During showering	-	-	-	-
	Contact with soil & dirt (e)	-	-	-	-
	From formaldehyde vapour in the air (f)	-	-	-	-
	TOTAL (Dermal)				

a.) Range of intakes is associated with the range of the 'mean' to '90th percentile' concentrations in outdoor air. It is to be noted that people are not exposed 24 hours to outdoor air. This estimation assumes 100 % exposure to outdoor air and is a measure of outdoor air quality per se and not of actual exposure.

b.) Range of intakes calculated from the 'mean' to '90th percentile' concentrations in outdoor air and assuming a 'typical' outdoor air exposure of = 3 hr(ie. corresponding to breathing 2.5 m<sup>3</sup>/3hr for adults and 0.63 m<sup>3</sup>/3hr for children.

c.) Range of intakes is estimated from the range of the lowest 'mean' and the highest '90th percentile' concentrations obtained from personal exposure and microenvironment measurements.

d.) Most of the formaldehyde is in *bound and unavailable form* (as per WHO see s. 3.2.1). This would suggest that the amount absorbed is limited but it is not possible to quantify the amount absorbed. The amount of food consumed by a child (<11y) is ~70% that of an adult. The adult intakes were multiplied by this percentage. The diets were considered to be similar.

e.) No data available, but intake is believed to be insignificant (see s 3.2.3 and 3.2.4.2)

f.) No permeability constants available (see s 3.2.4.3) and hence this exposure cannot be calculated.

g.) The intake shown is the direct intake of an adult smoker from smoking activity (ie. 'smoking') only. Various smoking environments for adults and children have already been included in the 'typical personal exposure' scenarios.

h.) The evidence points to close to 100 % absorption of formaldehyde (see s 1.1).

i.) See s. 3.2.2 regarding the uncertainty on the actual concentrations in Windsor drinking water.

Table 6. FORMALDEHYDE RISK CHARACTERIZATION in WINDSOR  
 Ranges of exposure guidelines, exposures and risk estimates  
 (Inhalation unless otherwise specified)

TB16FORM





5) Considering the information in Table 5 the exposures from the *non-inhalation* pathways are:

- *Ingestion* of food, water and soil:

adult - 1500 to 14000 ug/day

child - 1000 to 10000 ug/day

- *Dermal* absorption: Negligible

These ingestion exposures, dominated by exposure from food, are  $\approx$  5 to 10 times higher than from inhalation. It is to be noted that most of the formaldehyde is thought to be in a bound and unavailable form, that is, only some of the ingested formaldehyde is absorbed through the gastrointestinal tract. Furthermore, the carcinogenicity of formaldehyde by the oral route has not been unequivocally demonstrated and hence, for both of these reasons, it is not possible to determine the contribution of ingestion exposure to cancer risk.

Table 7. Range of Inhalation Cancer Risks Associated with Estimated Intakes  
(ie. for adult exposures only) of Formaldehyde

RANGE of INHALATION INTAKES			POTENCY (a)		RANGE of RISKS
Environment	Unit ug/day	Unit mg/kg/day	Agency	Unit (mg/kg-d) <sup>1</sup>	
OUTDOOR AIR QUALITY (Windsor)	72 - 152	$1.0 \times 10^{-3}$ - $2.2 \times 10^{-3}$	EPA('87)	$4.6 \times 10^{-2}$	$4.6 \times 10^{-5}$ - $1.0 \times 10^{-4}$
			EPA('91)	$2.1 \times 10^{-3}$	$2.1 \times 10^{-4}$ - $4.6 \times 10^{-4}$
			CDHS	$2.1 \times 10^{-2}$	$2.1 \times 10^{-5}$ - $4.6 \times 10^{-5}$
			NYSDOH	$6.1 \times 10^{-2}$	$6.1 \times 10^{-5}$ - $1.3 \times 10^{-4}$
			OVERALL RANGE OF RISKS: $2.1 \times 10^{-4}$ - $1.3 \times 10^{-4}$		
TYPICAL OUTDOOR EXPOSURE (ie.= 3 hr.)	9 - 19	$1.3 \times 10^{-4}$ - $2.7 \times 10^{-4}$	EPA('87)	$4.6 \times 10^{-2}$	$6.0 \times 10^{-4}$ - $1.2 \times 10^{-5}$
			EPA('91)	$2.1 \times 10^{-3}$	$2.7 \times 10^{-7}$ - $5.7 \times 10^{-7}$
			CDHS	$2.1 \times 10^{-2}$	$2.7 \times 10^{-4}$ - $5.7 \times 10^{-4}$
			NYSDOH	$6.1 \times 10^{-2}$	$7.9 \times 10^{-4}$ - $1.6 \times 10^{-5}$
			OVERALL RANGE OF RISKS: $2.7 \times 10^{-7}$ - $1.6 \times 10^{-5}$		
TYPICAL PERSONAL EXPOSURES	370 - 1029	$5.3 \times 10^{-3}$ - $14.7 \times 10^{-3}$	EPA('87)	$4.6 \times 10^{-2}$	$2.4 \times 10^{-4}$ - $6.8 \times 10^{-4}$
			EPA('91)	$2.1 \times 10^{-3}$	$1.1 \times 10^{-5}$ - $3.1 \times 10^{-5}$
			CDHS	$2.1 \times 10^{-2}$	$1.1 \times 10^{-4}$ - $3.1 \times 10^{-4}$
			NYSDOH	$6.1 \times 10^{-2}$	$3.2 \times 10^{-4}$ - $9.0 \times 10^{-4}$
			OVERALL RANGE OF RISKS: $1.1 \times 10^{-5}$ - $9.0 \times 10^{-4}$		
a. These are equivalent potency factors calculated from the unit risks proposed by the agencies listed; assumed adult weight of 70 kg and 20 m <sup>3</sup> per day.					

## Regulatory compliance messages:

6) The risk characterization in Table 6 indicates that, for the inhalation receptor exposures considered:

- The exposures potentially associated with outdoor air quality, for adults, youth and children, fall in the high range of the air quality guidelines of various jurisdictions.
- Exposures associated with typical outdoor exposure (ie.3 hr) is in the lowest 20 % of the air quality guidelines of various jurisdictions
- Exposures associated with personal activity patterns exceed the air quality guidelines of various jurisdictions.

It should be noted that these air quality guidelines may be of different types. Some are purely health based and some are regulatory and therefore may have been influenced by various risk management considerations. The regulatory guidelines may also have different uses (eg. judging the acceptability of air quality per se or judging the incremental addition by a source to the existing air quality).

7) All the inhalation exposures, including those associated with personal activity patterns are below the target level for residential indoor air quality, developed by the Federal-Provincial Committee on Environmental and Occupational Health.

8) Table 6 also indicates that all the inhalation exposures are less than the range of occupational levels.

9) The amount of formaldehyde that may be ingested (ie. range of 1000 to 14000 ug/day in Table 5) is less than the US-EPA oral RfD of 0.2 mg/kg-day (ie. an 'allowable' intake of 14000 ug/day). This oral RfD (ie. from Table 1; not shown in Table 6) was set to prevent systemic, non-carcinogenic effects.

10) MOEE is presently reviewing the basis of the existing standard for formaldehyde.

## Summary and recommendations:

♦ All the inhalation exposures overlap with or exceed the range of chronic acceptable exposure levels. Therefore, there is a possibility of long-term health effects, other than cancer risk, associated with all the inhalation exposures. Because of the possibility of long-term health effects, it is recommended that formaldehyde should be considered a candidate for reduction of exposure.

♦ Based on the most recent 1991 information from the US EPA, the range of estimated inhalation risks associated with 'outdoor air quality' (ie. 100% outdoor exposure) is between  $2.1 \times 10^{-6}$  and  $4.6 \times 10^{-6}$ . Similarly the range of risks associated with 'typical personal exposures' is between  $1.1 \times 10^{-5}$  and  $3.1 \times 10^{-5}$ . Since these levels of risk exceed  $1 \times 10^{-5}$ , a level generally deemed to be negligible, it is recommended that formaldehyde be considered a candidate for reduction of exposure

♦ Exposures and therefore risks associated with 'typical personal exposures' are slightly higher than the risks associated with 'outdoor air quality'.

♦ The commuting and smoke-affected indoor environments are the most dominant in the upper range of 'typical personal exposures'.

♦ The exposure that a smoker experiences overlaps with and exceeds the exposures associated with the personal activity patterns and substantially exceeds exposures associated with 'outdoor air quality'.

♦ Dermal exposures are considered negligible.

♦ Ingestion exposures, dominated by exposure from food, are  $\approx$  5 to 10 times higher than from inhalation. Most of the formaldehyde is thought to be in a bound and unavailable form, that is, only some of the ingested formaldehyde is absorbed through the gastrointestinal tract. Furthermore, the carcinogenicity of formaldehyde by the oral route has not been unequivocally demonstrated and hence, for both of these reasons, it is not possible to determine the contribution of ingestion exposure to cancer risk. The amount of formaldehyde that may be ingested is less than the US-EPA oral RfD which was set to prevent systemic, non-carcinogenic effects.

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## APPENDIX 5

### RISK ANALYSIS FOR 1,4 - DICHLOROBENZENE



## APPENDIX 5

### RISK ANALYSIS FOR 1,4 - DICHLOROBENZENE

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## 1,4 - DICHLOROBENZENE

### DESCRIPTION and SOURCES of 1,4 - DICHLOROBENZENE.

1,4 - Dichlorobenzene (ie. para- Dichlorobenzene, *p*- DCB) is a solid at room temperature with a strong odour resembling the smell of mothballs. When exposed to the air it slowly changes from its solid state into a vapour (ie. sublimes). It is used to make mothballs, deodorant blocks for restrooms and is used for controlling odours in animal holding facilities. 1,4 - Dichlorobenzene does not occur naturally, but is produced by chemical companies for various home/indoor uses. Most 1,4 - dichlorobenzene enters the environment as a result of its uses in moth repellent products and in toilet deodorizer blocks. Because it evaporates easily, almost all of what is produced is released into the air, mostly in the home. Some is released by factories that make or use it.

In 1990, in the U.S., approximately 132 million pounds of 1,4 - dichlorobenzene was produced. Production has increased during the past 10 years at a rate of about 2 % per year and this is expected to continue over the next few years at a rate of 2-4% per year.

### 1. HAZARD IDENTIFICATION

An extensive review on the toxicology, human epidemiology, environmental fate, and properties of 1,4-dichlorobenzene was published recently by the Agency for Toxic Substance and Disease Registry (ATSDR) of the US Department of Health and Human Services, Public Health Service<sup>1</sup>. The review, which encompasses past and recent findings obtained from a detailed literature search, provides an excellent integrative and interpretative evaluation of the 1,4-dichlorobenzene issue as related to its potential health effects on humans following exposure through various environmental pathways. As it is the scope of the current document to provide a general, although comprehensive updated overview on the toxicology of 1,4-dichlorobenzene, excerpts of the recent ATSDR document were used in the following sections to summarize the information considered to be of relevance for the Windsor study. A more detailed discussion of the health effects of 1,4-dichlorobenzene may be obtained by consulting references contained in section 5<sup>1-4</sup>.

#### 1.1 Absorption and Metabolism

Inhalation is the predominant route of exposure to 1,4-dichlorobenzene for the general population. Results from the TEAM study<sup>5</sup> in the United States have also revealed that 1,4-dichlorobenzene levels in indoor air are approximately 25 times higher than those found outdoor as a result of consumer products uses. On the other hand, the concentrations of 1,4-dichlorobenzene found in surface water, groundwater, and finished drinking water are generally negligible.

Little information is currently available to allow an evaluation of the rate and extent of absorption of 1,4-dichlorobenzene by the pulmonary, oral, and dermal routes in both experimental animals and humans. Comparative studies in rodents using the inhalation, gavage, and subcutaneous routes might suggest that pulmonary bioavailability is approximately 20%. However, differences in experimental protocols render this value questionable, and therefore no conclusions have been attempted at this point in time. The conservative assumption of 100% bioavailability may thus be acceptable under such circumstances. The US EPA has assumed 100% bioavailability by the oral route based on the absorption rates of benzene and of the smaller chlorinated aliphatics. Finally, no values are available for dermal uptake.

Evidence from animal studies indicates that the distribution of 1,4-dichlorobenzene is similar following inhalation, oral, or subcutaneous exposure. Fat tissues show high concentrations immediately after exposure, followed by kidney and liver for which the concentrations of 1,4-dichlorobenzene are

approximately 5-10% of those measured in fat tissues. Minimal amount can also be found in blood, lung, heart, and brain. The clearance of 1,4-dichlorobenzene from these organs, with the exception of fat tissues, appears to be rapid (no concentrations detected after 48 hours). Some human results are available from monitoring studies and post-mortem analysis of tissue samples that confirm the propensity of 1,4-dichlorobenzene to concentrate in fat tissues. Of major importance also is the detection of significant amounts of this chemical in breast milk of lactating women, thus indicating exposure of newborns.

Metabolism of 1,4-dichlorobenzene in both animals and humans seems to result mainly in the formation of 2,5-dichlorophenol which is excreted in the urine as glucuronic and sulfate conjugates. Other minor metabolites have also been detected although their identity is still unknown. Of major interest here is the observation that 1,4-dichlorobenzene is not mutagenic in microbial and mammalian systems, suggesting absence of formation of certain metabolites (e.g., oxide formation) generally associated with arene-based molecules.

As previously mentioned, 1,4-dichlorobenzene is excreted in the urine as conjugated forms, irrespective of the exposure route, and with only minor amounts (0.5-1%) being excreted in the breath.

## 1.2 Toxicology

Little information is available on the long-term effects induced by the inhalation of 1,4-dichlorobenzene in both experimental animals and humans. ATSDR<sup>1</sup> reports two cases of death by massive hepatic necrosis (fulminant hepatitis) of a 60-year-old man and his wife who had been exposed for several months to high concentrations of 1,4-dichlorobenzene (levels unknown). A case of pulmonary granulomatosis was reported to occur in a 53-year-old woman who for 12-15 years had been inhaling 1,4-dichlorobenzene crystals that were scattered on a weekly basis on the carpets and furniture of her home. Histological analysis of biopsy samples revealed fibrosis, thickening of the alveolar walls, and the presence of lymphocytes and histiocytes. It was suggested that these effects were caused by physical interactions of the crystals rather than by the chemical toxicity of 1,4-dichlorobenzene. In this case also, no information was available regarding the levels of exposure experienced by the subject. Animal experiments may provide some clues at this effect as suggested by studies that have reported interstitial edema, congestion and alveolar hemorrhage in the lungs of male rats, female guinea pigs, and rabbits exposed for 16 days at 173 ppm of 1,4-dichlorobenzene. Some of these effects may precede the pathologies discussed above. However, implications related to the physical nature of 1,4-dichlorobenzene (i.e., crystal *vs* aerosol), and their effects on the lung tissue (e.g., pulmonary granulomatosis following aerosol exposure) has not been addressed. Evidence also exists to indicate that inhalation of 1,4-dichlorobenzene produces immunological and neurological effects, while results regarding developmental and reproductive effects are inconclusive. The information on the effects induced by airborne 1,4-dichlorobenzene is summarized in Figure 1.1.

A substantially higher amount of experimental information is available on the effects induced by 1,4-dichlorobenzene following oral exposure in rodents. In humans, however, only limited qualitative information is available on hematological, dermal, and neurological effects. These effects have not been reproduced in studies where animals were chronically exposed by gavage to various doses of 1,4-dichlorobenzene. The most relevant study available to address the long-term effects induced by oral exposure to 1,4-dichlorobenzene in animals is the chronic gavage bioassay in mice and rats performed by the National Toxicology Program<sup>2</sup>. These studies have reported several effects affecting the lungs, kidneys, liver, and the hematopoietic system (see Figure 1.2). Of these, the most sensitive adverse response appeared to be induced in the kidneys and included nephropathy, epithelial hyperplasia of the renal pelvis, mineralization of the collecting tubules in the renal medulla, and focal hyperplasia of the renal tubular epithelium. Porphyria has also been observed in liver at doses of 50 mg/kg-day. This, however, was not accompanied by significant excretion of these substances in urine. Increases in hepatic enzyme activities have also been reported to occur at doses as low as 10 mg/kg-day. These effects,

Effects in Humans

PPM

Effects in Animals

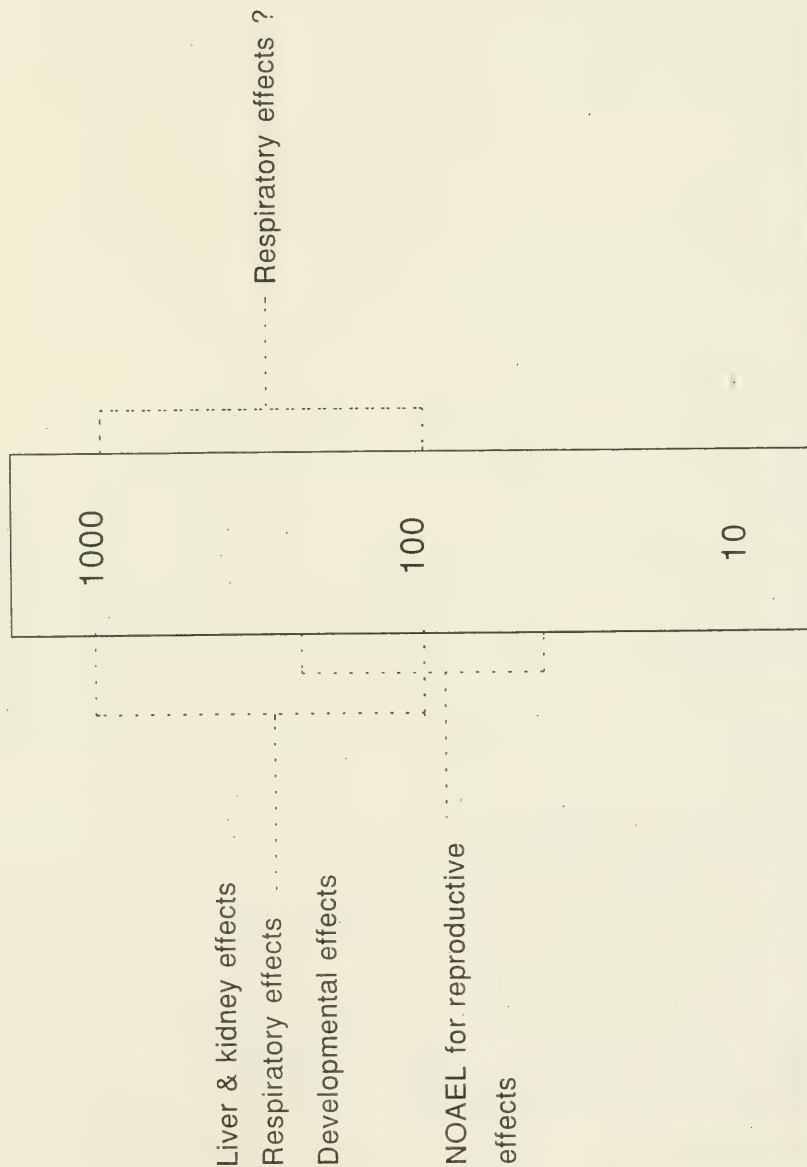


Figure 1.1 Summary of chronic effects associated with the inhalation of various concentrations of 1,4-dichlorobenzene (adapted from 1)(1ppm corresponds to 6.01 mg/m<sup>3</sup>)

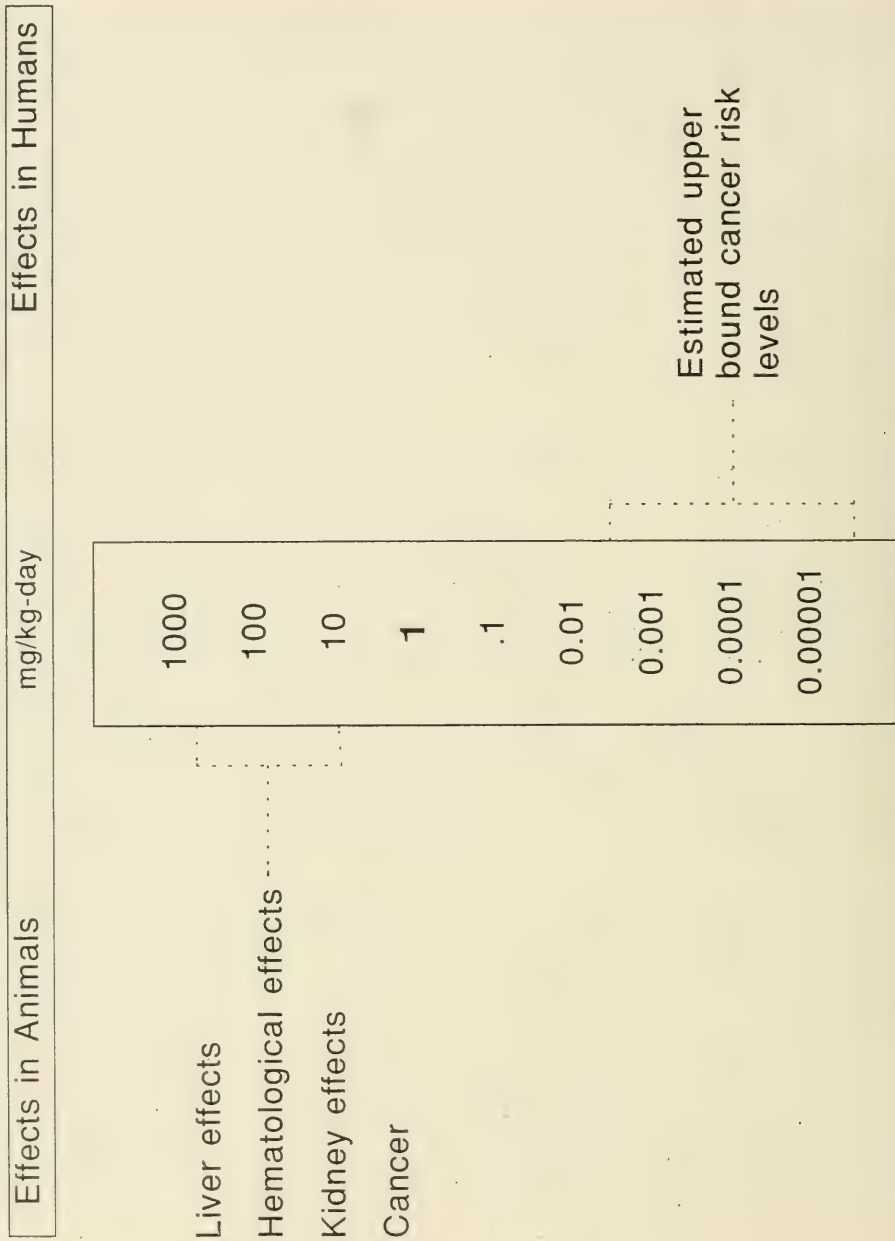


Figure 1.2 Summary of chronic effects associated with oral exposure to various doses of 1,4-dichlorobenzene (adapted from 1)



however, are generally considered adaptive mechanisms and may not bear pathologic consequences in the exposed animals.

1,4-dichlorobenzene has tested negative in various genotoxicity bioassays. Hence, unscheduled DNA synthesis (UDS) was not detected in mouse hepatocytes and rat renal tissues following gavage exposure, although significant increases in the DNA replication (S-phase of cell division) were noted. Clastogenic activity was also absent in mouse bone marrow erythroblasts following administration of 2500 mg/kg 1,4-dichlorobenzene, and 1500 mg/kg 2,5-dichlorophenol, the main metabolite of 1,4-dichlorobenzene. Finally, cytogenetic effects (including micronuclei) were not found in bone marrow cells of rodents exposed during a 13-week study. Studies conducted by the NTP<sup>3</sup> indicates that 1,4-dichlorobenzene was not mutagenic in *Salmonella typhimurium* strains TA98, TA100, TA1535, and TA1537.

Despite the absence of genotoxicity, 1,4-dichlorobenzene has been shown to be a multiple site carcinogen in both male and female mice and rats exposed by gavage for 2 years. Tumors were observed mainly in the kidneys of male rats (renal tubular cells adenocarcinomas), and in the liver of male and female mice (hepatocellular adenomas and carcinomas). There was also evidence of tumors of the sympathetic preganglia of the adrenal medulla in male mice. Finally, marginal increases of mononuclear cells leukemia were also reported. These neoplastic transformations were accompanied by various non-neoplastic effects such as hyperplasia of the thyroid gland follicles and adrenal gland medulla.

1,4-dichlorobenzene has been classified in Group 2B (Possibly carcinogenic to humans) by the International Agency for Research on Cancer (IARC)<sup>5</sup>; Group A2 (suspected human carcinogen, proposed) by the American Conference of Governmental Industrial Hygienists (ACGIH)<sup>7</sup>; and Group 2 (reasonably anticipated to be a carcinogen) by the National Toxicology Program (NTP)<sup>6</sup>. On the other hand, the evidence on the carcinogenicity of 1,4-dichlorobenzene is currently under review by the US EPA<sup>8</sup> and, consequently, no definitive information is available.

## 2. DOSE-RESPONSE INFORMATION/CURRENT EXPOSURE GUIDELINES

The uncertainties surrounding the potential toxicological effects of environmental 1,4-dichlorobenzene on communities have influenced the methodologies used to set guidelines and permissible exposure levels. As noted previously, the adoption of reasonably conservative assumptions is warranted in this context in order to provide sufficient protection of public health. This section summarizes various health criteria values, that is, exposure guidelines and dose-response information that leading regulatory agencies (and other relevant sources) have proposed and consider appropriate for permitting, assessing, and characterizing risks associated with various exposures. Potential exposures to 1,4-dichlorobenzene are evaluated in section 3 and the risk characterization is presented in section 4.

It is important to note that uncertainty exists presently on the relevance of the currently available permissible levels for 1,4-dichlorobenzene as a result of the review undertaken by various jurisdictions and regulatory agencies, including the Carcinogen Assessment Group (CAG) of the US EPA. Consequently, the information reported in the following sections should be considered provisional until more definitive information becomes available.

### 2.1 Air Guidelines

#### 2.1.1 Chronic, Non-Carcinogenic Health Effects

The US EPA's Integrated Risk Information System (IRIS) database<sup>8</sup> notes that the inhalation Reference Concentration (RfC) for 1,4-dichlorobenzene is not available at this time as a review is underway. On the other hand, a recent issue of the Health Effect Assessment Summary Tables (HEAST)<sup>9</sup> published by the

Office of Research and Development, Office of Emergency and Remedial Response of the US EPA indicates a *provisional* RfC value of 0.7 mg/m<sup>3</sup> for both chronic and sub-chronic effects. This value, which is purported to prevent liver and kidney effects, was derived based on inhalation studies in rats. HEAST notes, however, that these numbers are under review and that they are subject to change. The RfC, as defined by the US EPA, is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime.

The inhalation chronic AEL (Acceptable Exposure Level) for 1,4-dichlorobenzene adopted by the State of California (CDHS)<sup>10</sup> is the value proposed in the HEAST tables (0.7 mg/m<sup>3</sup>). Acceptable Exposure Levels (AELs) have the same purpose as the US EPA's RfC, *i.e.*, they are used for the evaluation of the potential noncancer adverse health effects of long-term (chronic) exposures.

The Massachusetts Department of Environmental Protection (MDEP)<sup>11</sup> has proposed in 1990 a Threshold Effects Exposure Limit (TEL) of 0.12 mg/m<sup>3</sup>, based on the ACGIH occupational exposure guideline<sup>7</sup>. This value is purported to prevent acute and (unspecified) chronic adverse effects. In view of the recognized carcinogenicity of 1,4-dichlorobenzene in animals, the TLV-TWA of 75 ppm (451 mg/m<sup>3</sup>) has been placed on the TLV Notice of Intended Changes in 1991 with a proposed TWA value of 10 ppm. This should not affect the current TEL limit value which was set to prevent non-carcinogenic health effects. However, the TEL value should also be considered provisional in view of the current review underway at the US EPA.

No ambient air guidelines for 1,4-dichlorobenzene have been suggested by the New York State Department of Environmental Conservation (NYSDEC)<sup>12</sup>, and by Calabrese and Kenyon<sup>13</sup> in their treatise on air toxics.

Generally, the inhalation chronic AEL, TEL, and the inhalation RfC noted above are comparable in their use for assessing chronic effects (except carcinogenic effects) due to inhalation. It is expected that constraining environmental exposures of human populations to cancer-preventive levels of 1,4-dichlorobenzene should decrease to negligible levels, or simply eliminate depending on the end-point of concern, the probability of occurrence of chronic non-cancer health effects.

### 2.1.2 Carcinogenic effects

Within the context of the current review underway at the US EPA, no inhalation unit risk factor for 1,4-dichlorobenzene is currently reported in the US EPA's Integrated Risk Information System (IRIS) database<sup>8</sup>. No unit risk factor is available in the HEAST<sup>9</sup> tables which, on the other hand, provide a *provisional* oral slope factor based on gavage studies in mice. No indication was given on whether this oral slope factor could be converted into an inhalation unit risk factor based on simple assumptions of weight and breathing rate, although absence of such values may suggest that considerations related to response differences as a function of exposure routes may have been considered by the authors. As previously noted, values for 1,4-dichlorobenzene contained in the HEAST tables are subject to change.

The California Department of Health Services (CDHS)<sup>7</sup> has established an inhalation unit risk of  $1.1 \times 10^{-5}$  (ug/m<sup>3</sup>)<sup>-1</sup> associated with lifetime continuous exposure to 1 ug/m<sup>3</sup>. No rationale was available in the above referenced document for the derivation of this value.

The Massachusetts Department of Environmental Protection (MDEP)<sup>11</sup> proposed an Allowable Ambient Limit (AAL) of 0.18 ug/m<sup>3</sup>. This value was obtained from a unit risk factor of  $5.7 \times 10^{-6}$  (ug/m<sup>3</sup>)<sup>-1</sup>, calculated based on a oral slope factor of  $2.13 \times 10^{-2}$  (mg/kg-day)<sup>-1</sup>. The oral slope factor, which is comparable to that reported in the HEAST<sup>9</sup> tables, was obtained using the incidence of male mouse liver tumors from the NTP<sup>3</sup> chronic gavage bioassay.

Air guidelines have also been proposed by other US states<sup>1</sup> although their values are generally based on averaging times (15 min., 1 hr., 8 hr.) not considered to be appropriate for preventing cancer effects. A few 24 hr average values are also available from the states of South Carolina (4.5 mg/m<sup>3</sup>), Virginia (7.5 mg/m<sup>3</sup>), and Massachusetts (4.3 ug/m<sup>3</sup>). However, absence of toxicological rationales (*e.g.*, knowledge of end-points) and substantial differences in these guidelines preclude their use in the assessment of long-term effects of 1,4-dichlorobenzene on human populations.

No air guidelines have been proposed by the International Agency for Research on Cancer (IARC) and the World Health Organization<sup>1</sup>, and by the Ontario Ministry of the Environment.

Occupational exposure guidelines have been developed for 1,4-dichlorobenzene. In the US, the Time-Weighted-Average Permissible Exposure Limit (TWA-PEL), established by the Occupational Safety and Health Administration (OSHA)<sup>7</sup> is 75 ppm (451,000 ug/m<sup>3</sup>). OSHA also proposes a Short-Term Exposure Limit (STEL) of 110 ppm on the basis that a STEL is necessary to protect workers from the significant risks of eye damage, vertigo, and neuropathic effects. No reference is made, however, to the potential occurrence of cancer effects. The American Conference of Industrial Hygienists (ACGIH)<sup>7</sup> presently has a Threshold Limit Value-Time Weighted Average (TLV-TWA) of 75 ppm (451,000 ug/m<sup>3</sup>), and a STEL of 110 ppm set to prevent acute and chronic effects. However, in light of reported studies of human eye irritation at 1,4-dichlorobenzene concentrations as low as 17 ppm (102 mg/m<sup>3</sup>), systemic toxicity in rats, and the IARC classification as a possible human carcinogen, 1,4-dichlorobenzene was placed on the TLV Notice of Intended Changes in 1991 with a proposed TWA value of 10 ppm, no STEL, and classified as an A2 suspected human carcinogen.

An occupational guideline for 1,4-dichlorobenzene is currently not available in Ontario. The above guidelines for atmospheric 1,4-dichlorobenzene are summarized in Table 1 below.

## 2.2 Other Route Guidelines

There are no human studies regarding cancer effects after oral exposure to 1,4-dichlorobenzene. On the other hand, rodents fed 1,4-dichlorobenzene have developed kidney and liver tumors. It is generally assumed, in the context of guideline development, that humans also will develop tumors if 1,4-dichlorobenzene is ingested<sup>8</sup>.

Various guidelines and regulations are currently available for controlling the intake of 1,3-dichlorobenzene through drinking water. Little regulation, however, is available for contaminated food despite the fact that exposure to 1,4-dichlorobenzene may occur through the consumption of fish, sea food and other components of the food chain that bioconcentrate and biomagnify 1,4-dichlorobenzene<sup>1</sup>.

As previously discussed, for the purpose of estimating cancer risks from oral exposures the US EPA has reported in the HEAST<sup>9</sup> tables an oral slope factor of  $2.4 \times 10^{-2}$  (mg/kg-day)<sup>-1</sup> based on the incidence of mouse liver tumors derived from the NTP<sup>3</sup> chronic gavage bioassay. By assuming a daily intake of 2 L of water and an average weight of 70 kg, the drinking water unit risk factor was estimated at  $6.8 \times 10^{-7}$  (ug/l)<sup>-1</sup>. Therefore, an incremental upper bound lifetime risk of 1 in one million ( $10^{-6}$ ) of contracting liver cancer would be associated with a lifetime daily consumption of 2 L of water contaminated with 1.5 ug/L (1.5 ppb) of 1,4-dichlorobenzene. Conversely, an excess risk of 1 in 100,000 ( $10^{-5}$ ) would be associated with a concentration of 15 ug/L (15 ppb). The US EPA has also issued drinking water health advisories for the purpose of assessing short-term exposures only. These may not protect against cancer since they are generally higher than cancer-based guidelines and are intended primarily for emergency purposes.

In its 1992 risk assessment guidelines for air toxics, the California Air Pollution Control Officer Association (CAPCOA)<sup>10</sup> indicates that the oral potency value for 1,4-dichlorobenzene is  $4.0 \times 10^{-2}$  (mg/kg-day)<sup>-1</sup>. This



TABLE 1. Summary of Exposure Guidelines for 1,4-Dichlorobenzene from Leading Agencies

GUIDELINE APPLICATION	AGENCY(IES)	ORIGINAL VALUE	CONCENTRATION ("Original Form" converted to these -as applicable)			CALCULATED "ALLOWABLE" INTAKE (3)
			Unit Risk (1)	RsC (2) (1 x 10 <sup>-4</sup> )	RsC (2) (1 x 10 <sup>-4</sup> )	
INHALATION GUIDELINES						
Occupational	OSHA, ACGIH,	451000 ug/m <sup>3</sup>	NA	NA	NA	9020 mg/day (129)
Ambient Air Quality Guidelines	US states,	4.2 - 7500 ug/m <sup>3</sup>	NA	NA	NA	84 - 150000 (1.2 x 10 <sup>3</sup> - 2.1)
Ontario Air Quality Guideline	OMOE	NA	NA	NA	NA	NA
Chronic AELs/RfCs	CDHS, HEAST	120 - 700 ug/m <sup>3</sup>	NA	NA	NA	2400 - 14000 (0.03 - 0.20)
Inhalation Cancer Potency Factor	CDHS MDEP	See Unit Risk column	1.1 x 10 <sup>-6</sup> 5.7 x 10 <sup>-6</sup>	0.9 1.75	0.09 0.18	for 1 x 10 <sup>-5</sup> risk: 18 - 35 (2.6 x 10 <sup>-4</sup> - 5 x 10 <sup>-4</sup> ) for 1 x 10 <sup>-4</sup> risk: 1.8 - 3.5 (2.6 x 10 <sup>-5</sup> - 5 x 10 <sup>-5</sup> )
INGESTION GUIDELINES						
Drinking Water Guideline	Ontario, US states	5.0 - 75 ug/L	NA	NA	NA	7.5 - 112.5 (1.1 x 10 <sup>-4</sup> - 1.6 x 10 <sup>-3</sup> )
Oral Cancer Potency Factor	HEAST	2.4 x 10 <sup>-2</sup> (mg/kg-day) <sup>-1</sup>	6.8 x 10 <sup>-7</sup>	15	1.5	for 1 x 10 <sup>-5</sup> risk: 22.5 (3.2 x 10 <sup>-4</sup> ) for 1 x 10 <sup>-4</sup> risk: 2.2 (3.2 x 10 <sup>-5</sup> )

<sup>1</sup>For inhalation and ingestion guidelines, unit risks are expressed as (ug/m<sup>3</sup>)<sup>-1</sup> and (ug/L)<sup>-1</sup>, respectively

<sup>2</sup>For inhalation and ingestion guidelines, risk specific concentrations are expressed as ug/m<sup>3</sup> and ug/L, respectively

<sup>3</sup>Intake was computed by assuming, where applicable, an adult weight of 70 kg, a breathing rate of 20 m<sup>3</sup>/day, a water intake of 1.5 L/day. In all cases 100% bioavailability of the intake was assumed.

value was adopted from the 1991 HEAST tables, which have since been updated with the values reported above ( $2.4 \times 10^{-2}$  (mg/kg-day)<sup>11</sup>) and, therefore, its current relevance is questionable and it will not be used for the present exercise. The current drinking water quality standard enforced in California is 5 ug/L, which is the Practical Quantitation limit (PQL) based on the ability of laboratories to measure 1,4-dichlorobenzene with reasonable limits of precision and accuracy<sup>15</sup>. A similar value of 5 ug/L is reported for the State of Massachusetts<sup>1</sup>.

Several other jurisdictions have developed their own drinking water quality standards. However, it is doubtful that these values were derived based solely on health effects and analytical considerations. Difficulties associated with the implementation and enforcement of these values may be responsible for this situation. Hence, according to the most recent ATSDR document<sup>1</sup>, drinking water quality standards for the various jurisdictions cited which include the states of Alabama, Arizona, Connecticut, Maine, Minnesota, Rhode Island, Vermont, and Wisconsin, all have drinking water quality standards ranging from 27 to 75 ug/L.

The World Health Organization<sup>1</sup> has recommended a drinking water guideline of 0.1 ug/L, which appears to be 50 times lower than the PQL previously discussed.

Finally, the current Maximum Acceptable Concentration (MAC) in drinking water in Ontario is 5 ug/L based on toxicological, feasibility, and analytical considerations as summarized in the Canadian water quality guidelines handbook<sup>15</sup>. The above ingestion guidelines are summarized in Table 1.

### **3. HUMAN EXPOSURE ASSESSMENT**

#### **3.1 Inhalation**

##### **3.1.1 Ambient Air Quality**

Ambient levels of 1,4 - dichlorobenzene have been measured at five fixed site stations in Windsor by two monitoring agencies, the Ontario Ministry of Environment and Energy and the Environmental Protection Service of Environment Canada. The measurements include four years of data and 221 samples, each collected over a 24 hour period. Concentration levels range from non-detectable to 14.6 ug/m<sup>3</sup>, with the median, mean (average), 90th percentile and 95th percentile levels being 0.70, 1.30, 3.19 and 5.54 ug/m<sup>3</sup>, respectively<sup>14</sup>.

It is possible to estimate the daily intake of 1,4 - dichlorobenzene associated with these measures of Windsor ambient air quality, recognizing that personal real exposures/intakes may be quite different as further discussed in section 3.1.2. Table 2 below shows these estimated intakes for two different receptors, i.e., an adult and a child. It should be noted that these intakes were calculated based on 24 hour exposures and assume 100% bioavailability by the inhalation route.

##### **3.1.2 Microenvironments**

It is reasonable to assume that the daily 1,4 - dichlorobenzene intakes associated with typical personal exposure patterns will be different from those based on fixed site monitoring data. With most of the substances on the Windsor focus list, this evaluation was based on various microenvironmental concentrations. For the purpose of scoping population exposures, the set of typical receptors in Table 3 below was normally considered. Examples of the receptor types and/or their characteristics are also included in Table 3. For 1,4 - dichlorobenzene, Windsor-specific microenvironment and personal



**Table 2. Estimated Daily Intakes of 1,4 - Dichlorobenzene Associated With Ambient Air Quality in Windsor**

Air Quality Measure (a)	Concentration ug/m <sup>3</sup>	Adult (b) ug/day (ug/kg-day)	Child (b) ug/day (ug/kg-day)
Median	0.70	14.0 (0.2)	3.5 (0.2)
Mean	1.30	26.0 (0.4)	6.5 (0.4)
90th percentile	3.19	63.8 (0.9)	16.0 (1.1)
a) Based on 221, 24 hour average samples b) Assuming the following weights and inhalation rates per day (ie. per 24 hour period): Adult: 70 kg; 20 m <sup>3</sup> /day Child: 15 kg; 5 m <sup>3</sup> /day			

exposure concentrations were not available. As a surrogate, indoor concentrations acquired in other studies were used to represent the range of 'typical personal exposure' patterns. The concentration from these studies and the associated estimated daily intakes (in ug/day) are summarized in Table 4.

**Table 3. Receptors With Typical Personal Exposure Patterns**

NAME OF RECEPTOR TYPE	CHARACTERISTICS	NAME OF RECEPTOR TYPE	CHARACTERISTICS
Average Office Worker (Non-smoking)	Eg. - Typical office worker (Based on Windsor volunteers and US EPA TEAM study; not smoking at home)	High Outdoor Receptor	Eg. - Construction workers; - Bicycle couriers - Police - Long distance runners
Average Office Worker (Smoker Environment)	Eg. - Typical office worker (Based on Windsor volunteers and US EPA TEAM study; smoking at home)	High Indoor Receptor	Eg. - 'Shut-ins'- Invalids - Elderly, non-mobile
Average Youth	Eg. Special exposures at shopping malls and athletic facilities (pools) in addition to school;	High Commuting Receptor	Eg.- Bus drivers - Taxi drivers - Delivery/ Distribution Services
Average Child (Non-Smoker Home & No Exposure to Tobacco Smoke)	Eg. Similar to average office worker except 'School' replaces 'Office';	Active Receptor # 1	Eg- 7 hr/week in Bingo Hall or Bar

Average Child (Non-Smoker Home & Typical Exposure to Tobacco Smoke)	Eg. Includes typical times that children may be in proximity to tobacco smoke, outside the home, based on activity pattern studies;		
Average Child (Smoker Home with Exposure to Tobacco Smoke)	Eg. Child living in a house where there is a smoker		

Table 4. Estimated Daily Intakes of 1,4 - Dichlorobenzene Associated With Indoor Air Environments (ie. to represent 'Typical personal exposures').

Indoor Air Environment (a)	Concentration  ug/m <sup>3</sup>	Adult (b)  ug/day (ug/kg-day)	Child (b)  ug/day (ug/kg-day)
Mean (Range of means from 3 studies)	1.7 - 56*	34 - 1120 (0.5 - 16)	8.5 - 280 (0.6 - 18.7)
a) Based on three studies listed in: Agency for Toxic Substances and Disease Registry, U.S. Public Health Service, Toxicological Profile for 1,4 - Dichlorobenzene, February, 1992, p 69. b) Assuming the following weights and inhalation rates per day (ie. per 24 hour period): Adult: 70 kg; 20 m <sup>3</sup> /day Child: 15 kg; 5 m <sup>3</sup> /day			

A microenvironment, in which measurements were not taken, is the bathroom during bathing and showering.

Volatile organic chemicals will partition from the hot water during showering and bathing and be inhaled by the person in the bathroom. A simple one-compartment model has been developed that takes into account the air exchange between shower stall and bathroom and the rest of the house and calculates the maximum concentration -  $C_{amax}$  - reached during showering<sup>18</sup>. The formula is

$$C_{amax} = C_w f F_w t_d / V_a$$

where:  $C_w$  is the water concentration (ug/L)

$f$  is the fractional volatilization rate with an assumed value of 0.75 (range 0.5 - 0.9)

$F_w$  is the volume of water used (L/h)

$t_d$  is the time spent in the shower or bath (h)

$V_a$  is the volume of the shower stall or bathroom (L)

The shower stall is assumed to have a volume of 2 m<sup>3</sup> or 2000 L and the showering time is 0.25 h. The

average flow rate is 260 L/h and the upper bound is 720<sup>18</sup>. The estimated water concentration is <0.1 ug/L (s. 3.2.2). The maximum calculated air concentration is <2.4 ug/m<sup>3</sup> and the upper bound is <6.8 ug/m<sup>3</sup>.

The average concentration is approximately half that of  $C_{\text{max}}$  (assuming a linear increase with time). The average inhalation rate is 20 m<sup>3</sup>/d or 833 L/h. The average amount inhaled during the showering is then <0.26 ug and the maximum is <0.70 ug.

An alternative scenario as described by the authors assumes full exchange between the shower stall and the bathroom ( $V_s = 10 \text{ m}^3$ ), 15 minutes for a shower and an additional 15 minutes in the bathroom. The concentration during the shower is  $C_{\text{max}}/2$  and during the remaining 15 minutes is approximately  $C_{\text{ave}}$  (assuming the exchange with the rest of the house is slow). Under these circumstances,  $C_{\text{max}}$  is <0.49, with an upper bound of 1.35 ug/m<sup>3</sup> and the amounts inhaled are <0.15 and <0.42 ug. These calculations assume that 100% of the inhaled 1,4-dichlorobenzene is absorbed across the lung. Studies in rodents suggest that the pulmonary bioavailability is approximately 20% (s. 1.1).

Based on the above, maximum inhalation intakes per day, via the two possible scenarios above, are in the range of 0.15 to 0.70 ug/day. In view of the relatively small intake from this microenvironment compared to other inhalation intakes, this can be considered negligible.

In order to place the above inhalation exposures (ie. intakes) in Windsor in perspective, it is appropriate to examine the daily intakes that people who smoke may experience.

### 3.1.3 Smoking.

Cigarette smoke has been reported to contain trace quantities of simple chlorocarbons, but 1,4-dichlorobenzene is not suspected to be present in significant concentrations in either mainstream or sidestream smoke (Ref. 17, p.216 and table 11.2).

Furthermore, it is also important to place the inhalation exposures (ie. intakes) in Windsor into perspective, relative to general exposures from other media (ie. see s. 3.2).

## 3.2 Other Routes

In this section, possible non-inhalation routes of exposure (ie. ingestion and dermal) are assessed.

### 3.2.1 Ingestion of Food

1,4-dichlorobenzene has been reported in trout from the Great Lakes (1-4 ng/g) and in other fish and shellfish<sup>1</sup>. It is expected to bioconcentrate in aquatic organisms because of its high octanol/water partition coefficient ( $K_{\text{ow}} = 2500$ ). Measured bioconcentration factors for fish range from 400 to 1800 (Ref. 1, p.67). There are a few reports of the compound being found in pork and eggs, likely originating from its use for odour control. It is unlikely that food is a significant exposure pathway.

### 3.2.2 Drinking Water

1,4-dichlorobenzene was measured in the drinking water in Windsor. The concentration in 1990-1991 were all below the detection limit of 0.1 ug/L. It has been detected (Ref. 1, p.68) at very low levels in the Great Lakes (ie. 0.3 to 1.5 ng/L) and in the drinking water of three cities on Lake Ontario (ie. 8 - 20 ng/L). It

is expected to volatilize relatively rapidly from water bodies (Ref. 1, p.66). The intake from drinking water is expected to be <0.2 ug/d.

### 3.2.3 Soil

No data on 1,4-dichlorobenzene was collected during the Windsor study. It is expected to sorb to the organic matter in soils and sediments, but sorption is likely to be reversible and therefore it can be leached from the soil to groundwater. Based on its tendency to sublime, volatilization is most likely <sup>1</sup>.

### 3.2.4 Dermal

#### 3.2.4.1 During Showering and Bathing

EPA<sup>16</sup> has proposed a model for transient state dermal adsorption from water. The basic formula for organic compounds is, for  $t_{\text{event}} < t^*$

$$DA_{\text{event}} = 2K_p C_w (6\tau t_{\text{event}} / \pi)^{1/2}$$

where:  $DA_{\text{event}}$  is dose absorbed per unit area per event (mg/cm<sup>2</sup>event)

$K_p$  is the permeability coefficient (cm/hr)

$C_w$  is the concentration in the water (mg/cm<sup>3</sup>)

$t_{\text{event}}$  is the time spent showering or bathing (hr)

$\tau$  is a number calculated from the skin thickness and diffusivity of the chemical in the skin (hr)

$t^*$  is number that is calculated from the value of B (hr) ( $B = K_{ow}/10^4$ ;  $K_{ow}$  is the octanol/water partition coefficient)

Table 5-8 in US-EPA <sup>16</sup> gives the appropriate values to use in the above equation. For 1,4-dichlorobenzene, the estimated value for  $K_p$  is 0.062 cm/hr, for  $\tau$  is 0.69 hr and for  $t^*$  is 3.3 hr. Assuming that a shower takes 0.25 hr/d, a median skin surface area of 19400 cm<sup>2</sup> (table 8-3) for an adult and a water concentration of <0.1 ug/L (s.3.2.2), the amount absorbed during a shower is <0.04 ug. The amount absorbed during a bath of 0.5 hr duration would be <0.06 ug.

#### 3.2.4.2 Contact With Soil and Dirt

Since there is no data on the concentration in soil, the dermal absorption cannot be calculated.

#### 3.2.4.3 From 1,4 - Dichlorobenzene Vapour in the Air

The absorption through the skin of vapors in the air can be calculated from the formula (Ref. 16, p. 7-16):

$$DA_{\text{event}} = K_p^{\text{air}} C_{\text{air}} t_{\text{event}}$$

where:

$DA_{\text{event}}$  is the absorbed dose per event (mg/cm<sup>2</sup>-event)

$K_p^{\text{air}}$  is the permeability constant (cm/hr)

$C_{\text{air}}$  is the concentration of the vapor in air (mg/cm<sup>3</sup>)

$t_{\text{event}}$  is the exposure time (hr/event)

There does not appear to be a vapour permeability constant for 1,4-dichlorobenzene (Ref.16, chap.7), but the estimated value for chlorobenzene is 0.587 cm/hr and for benzene is 0.206 (Ref. 16, t.7-7). Two values are given for the permeability coefficient for benzene - 0.08 cm/hr (Ref. 2, table 7-1) and 0.206 (Ref. 2, table 7-7). The latter value is estimated from fat/air partition coefficients and the first one is measured experimentally. It is therefore likely that the permeability coefficient for chlorobenzene is also an overestimate.

From Table 4, the range in weighted air concentrations is 1.7 to 56 ug/m<sup>3</sup>. The higher value is likely in situations where the chemical is being used as a space deodorizer or moth repellent. The median surface area for an adult is 1.94 m<sup>2</sup> and for a child, 0.73. The exposure time is 24 hr.

Using the minimum and maximum values of the indoor concentrations and the permeability coefficient for chlorobenzene, the doses absorbed per day are:

adult : 0.5 to 15 ug  
child: 0.2 to 6 ug

#### 4.0 RISK CHARACTERIZATION AND PERSPECTIVES

Exposures, expressed as daily intakes in units of ug/day, were assessed in section 3. Inhalation, ingestion and dermal routes of exposure were considered. Table 5 below summarizes the daily intakes (or ranges of daily intakes) of 1,4 - dichlorobenzene, for adults and children, estimated in section 3. It should be noted that in section 3, the intakes for inhalation and sometimes for ingestion assumed 100% bioavailability. The intake for dermal exposures are amounts absorbed systemically and hence already include bioavailability considerations. Table 5 has two columns for both adults and children. The first set of columns (ie. '100 % Bioav') give the intakes with 100 % bioavailability having been assumed; the second set (ie. "Bioav. Incl."), gives intakes for which bioavailability has been taken into consideration (ie. if information was available as noted in the footnotes). This second set of columns should give a better picture of the relative importance of various exposure routes. As far as comparison to exposure guidelines and intakes associated with cancer risk, the intakes in the first set of columns of Table 5 will be used since the exposure guidelines are also expressed as intakes for which we have assumed 100 % bioavailability.

To characterize risks, the various exposure guidelines discussed in Section 2 are compared to the estimated exposures from inhalation and other routes as discussed in Section 3. Because of the assumptions, uncertainties and ranges of values available from both exposures (see Table 5) and the various exposure



guidelines (see Table 1), risk characterization is most appropriately done by comparison of ranges of values.

Table 6 below provides a graphic representation of this comparison of exposures, exposure guidelines and intakes associated with inhalation cancer risk, based on ug intake/day (ie. 'INTAKE in Micrograms per day' increasing upwards on the vertical scale).

The middle section of Table 6, "Exposures", depicts the exposures calculated in Section 3, expressed as intake/day (ie. ug/day). The exposures depicted are: *Outdoor Air Quality* - the exposure from spending 100 % of the day outdoors; *Typical Outdoor Exposure* - the exposure from three hours only outdoors, provided for perspective on the contribution to risk solely from contaminants present in outdoor air; *Typical Personal Exposures* - the range of exposures associated with 'personal activity patterns' (ie. for this chemical, surrogate indoor air values were used because of the lack of Windsor specific data) combining periods of indoor, outdoor and various microenvironment exposures. Exposure scenarios are included for adults and children, assuming 20 and 5 m<sup>3</sup>/day inhalation rates respectively. For 'outdoor air quality' (ie. 100% outdoor exposure), for 'typical outdoor exposures' (ie. 3 hr), and for the 'typical activity patterns' the ranges shown, bracket the lowest mean to the highest 90th percentile. For the 'personal activity patterns' - ie. indoors' the range indicates the overall range of possible exposures (see s. 3.1.2 and Table 4).

The left section of Table 6, "Exposure Guidelines", expresses the various guidelines discussed in Section 2 in terms of calculated "allowable" intake/day for adults and children. The values are taken from Table 1. Within each type of guideline group (eg. outdoor air) ranges of exposure guidelines, when available, are indicated. Thus, ranges of Air Quality Guidelines (ie. 'Outdoor Air'), Occupational guidelines (ie. 'Workplace Air'), and chronic health effects based reference concentrations (ie. 'Chronic AEL') are shown. Comparison of "Exposure Guidelines" to "Exposures" should be done with care. For example, occupational guidelines are included for perspective purposes only. For caveats regarding this comparison see section 4.1.1 of the main report.

The right section of Table 6, "Intakes Associated With Cancer Risk", shows the intakes associated with different levels of cancer risk. Ranges of carcinogenic risk levels (associated with  $1 \times 10^{-5}$  risk and  $1 \times 10^{-6}$  risk) are depicted. The provisional nature of these inhalation risks is noted in observation # 5 below. Comparison of "Exposures" to "Intakes Associated With Cancer Risk" is appropriate for adult exposures only, since cancer risk estimates apply to a lifetime of exposure and people are adults for the majority of their lives. Adult exposures in the bars of the "Exposure" section fall in the top 70 % of the bars which represent exposures of adults and children.

Based on the tabular analysis (Table 5) and the graphic risk characterization (Table 6), the following observations and deductions can be made:

#### Health messages:

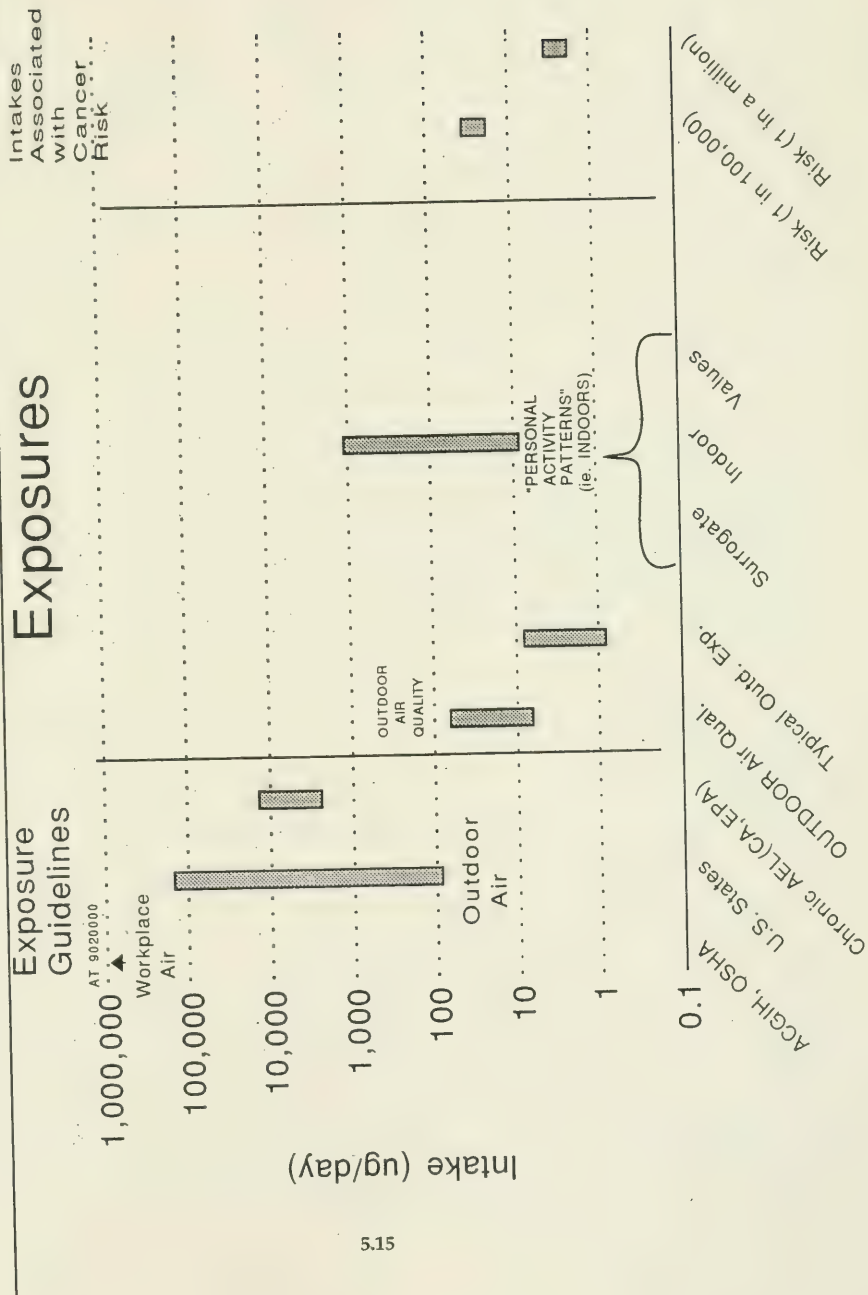
1) It is apparent, that the inhalation route generally exceeds all other exposure routes for 1,4-dichlorobenzene. Exposure by ingestion and via the skin are less. Dermal exposure appears to be slightly more important than ingestion.

2) All the inhalation exposures are less than the range of available chronic acceptable exposure levels - 'Chronic AEL(CA, EPA)' - (ie. range is 2400-14000 ug/day from Table 1) proposed by California (CDHS) and EPA. These chronic acceptable exposure levels are considered to be purely health based and are protective against all chronic health effects other than cancer risk. Therefore, the possibility of long-term health effects, other than cancer risk, is unlikely.

Table 5. Summary of Estimated Daily Intakes and/or Range of Intakes (in ug /day), from Various Exposure Pathways (ie. intakes, assuming 100 % bioavailability and intakes with bioavailability taken into consideration)

EXPOSURE PATHWAY		ADULT ug/day  (100 % Bioav.)	ADULT ug/day  (Bioav. Incl.)	CHILD ug/day  (100 % Bioav.)	CHILD ug/day  (Bioav. Incl.)
INHALATION	Outdoor Air Quality - Windsor (ie. 100 % outdoor exposure)(a)	26.0 - 63.8	26.0 - 63.8 (h)	6.5 - 16.0	6.5 - 16.0 (h)
	Typical outdoor exposure (ie. = 3hr)(b)	3.3 - 8.0	3.3 - 8.0 (h)	0.8 - 2.0	0.8 - 2.0 (h)
	Typical personal exposures(ie. Table 4/Surrogate indoor values) (c)	34 - 1120	34 - 1120 (h)	8.5 - 280	8.5 - 280 (h)
	Smoking (e)	-	-		
INGESTION	Food (d)	-	-	-	-
	Drinking water	<0.2	<0.2 (h)	<0.2	<0.2 (h)
	Soil (f)	-	-	-	-
	TOTAL (Ingestion)	<0.2	<0.2	<0.2	<0.2
DERMAL	During showering		<0.06		<0.06
	Contact with soil & dirt (f)		-		-
	From 1,4 - dichlorobenzene vapour in the air (g)		0.5 - 15		0.2 - 6
	TOTAL (Dermal)		0.5 - 15		0.2 - 6
<p>a.) Range of intakes is associated with the range of the 'mean' to '90th percentile' concentrations in outdoor air. It is to be noted that people are not exposed 24 hours to outdoor air. This estimation assumes 100 % exposure to outdoor air and is a measure of outdoor air quality per se and not of actual exposure.</p> <p>b.) Range of intakes calculated from the 'mean' to '90th percentile' concentrations in outdoor air and assuming a 'typical' outdoor air exposure of = 3 hr(ie. corresponding to breathing 2.5 m<sup>3</sup>/3hr for adults and 0.63 m<sup>3</sup>/3hr for children.</p> <p>c.) Range of intakes is estimated from the range of the 'mean' concentrations obtained from indoor air studies. These were assumed to represent the range of intakes associated with 'typical personal exposure' patterns.</p> <p>d.) Unlikely to be a significant pathway (s. 3.3.1)</p> <p>e.) Not believed to be present in significant amounts in tobacco smoke (s 3.1.3.</p> <p>f.) No data on soil concentrations (s. 3.2.3)</p> <p>g.) Exposures estimated using the permeability constant for chlorobenzene (s. 3.2.4.3).</p> <p>h.) For both inhalation and ingestion an absorption rate of 100 % was assumed (see s. 1.1)</p>					

Table 6. 1,4-DICHLOROBENZENE RISK CHARACTERIZATION in WINDSOR  
 Ranges of exposure guidelines, exposures and risk estimates  
 (Inhalation unless otherwise specified)



This comparison of exposures to chronic acceptable exposure levels can also be expressed more quantitatively in the form of a hazard index. These hazard index comparisons for all substances are summarized and are found in section 4.1.5 of the main report.

3) The most conservative range of available exposure guidelines are depicted in Table 6 under Intakes Associated with Cancer Risk. These guidelines were proposed by CDHS and MDEP. As shown in Table 6, they overlap with and are exceeded by the estimated exposures. Because people are adults for the majority of their lives, these intakes associated with cancer risk are depicted for adults only. The inhalation intakes for adults associated with 'outdoor air quality' (ie. 100 % outdoor exposure), 'typical outdoor exposure' (ie. 3 hr) and 'typical personal exposures' range between 26 - 64 ug/day, 3.3 - 8 ug/day and 34 - 1120 ug/day, respectively (from Tables 2, 4 and 5). These intakes and the corresponding doses in mg/kg-day are summarized in Table 7. Using the various potencies from the two agencies, the range of risks associated with 'outdoor air quality' (ie. 100% outdoor exposure) is between  $7.4 \times 10^{-6}$  and  $3.6 \times 10^{-5}$ . Similarly the range of risks associated with 'typical outdoor exposures' (ie. 3 hr) is between  $9.4 \times 10^{-7}$  and  $4.3 \times 10^{-6}$ . Similarly the range of risks associated with 'typical personal exposures' is between  $9.8 \times 10^{-6}$  and  $6.2 \times 10^{-4}$ . The risks associated with 'typical personal exposures' are higher than the risks associated with 'outdoor air quality' which in turn is higher than 'typical outdoor exposures'. This range of risk analysis is summarized in Table 7. It should be further noted, that this risk characterization (ie.

**Table 7. Range of Inhalation Cancer Risks Associated with Estimated Intakes (ie. for adult exposures only) of 1,4 - Dichlorobenzene**

RANGE of INHALATION INTAKES			POTENCY (a)		RANGE of RISKS
Environment	Unit ug/day	Unit mg/kg/day	Agency	Unit (mg/kg-d) <sup>1</sup>	
OUTDOOR AIR QUALITY (Windsor)	26 - 64	$3.7 \times 10^{-4}$ - $9.1 \times 10^{-4}$	EPA	NA	
			CDHS	$3.9 \times 10^{-2}$	$1.4 \times 10^{-5}$ - $3.6 \times 10^{-5}$
			MDEP	$2.0 \times 10^{-2}$	$7.4 \times 10^{-6}$ - $1.8 \times 10^{-5}$
			OVERALL RANGE OF RISKS: $7.4 \times 10^{-6}$ - $3.6 \times 10^{-5}$		
TYPICAL OUTDOOR EXPOSURE (ie.= 3 hr.)	3.3 - 8	$4.7 \times 10^{-5}$ - $1.1 \times 10^{-4}$	EPA	NA	
			CDHS	$3.9 \times 10^{-2}$	$1.8 \times 10^{-6}$ - $4.3 \times 10^{-6}$
			MDEP	$2.0 \times 10^{-2}$	$9.4 \times 10^{-7}$ - $2.2 \times 10^{-6}$
			OVERALL RANGE OF RISKS: $9.4 \times 10^{-7}$ - $4.3 \times 10^{-6}$		
TYPICAL PERSONAL EXPOSURES	34 - 1120	$4.9 \times 10^{-4}$ - $1.6 \times 10^{-3}$	EPA	NA	
			CDHS	$3.9 \times 10^{-2}$	$1.9 \times 10^{-5}$ - $6.2 \times 10^{-4}$
			MDEP	$2.0 \times 10^{-2}$	$9.8 \times 10^{-6}$ - $3.2 \times 10^{-4}$
			OVERALL RANGE OF RISKS: $9.8 \times 10^{-6}$ - $6.2 \times 10^{-4}$		
a. These are equivalent potency factors calculated from the unit risks proposed by the agencies listed; assumed adult weight of 70 kg and 20 m <sup>3</sup> per day. See observation # 3 regarding the provisional nature of these inhalation potency factors.					

using carcinogenic risk based limits) is based on an assumed lifetime exposure (ie, 24 hours, every day, for 70 years) and hence is a very conservative assumption. It should also be noted that oral potencies (based on oral gavage studies) were used by both CDHS and MDEP, and in turn, in the risk estimates in



Table 7, to calculate inhalation unit risks and the corresponding inhalation potency factors. Hence these risk estimates are considered provisional (see s. 2.1.2).

- 4) 1,4-Dichlorobenzene exposure from smoking is not expected to be significant.
- 5) Considering the information in Table 5, the exposures from the *non-inhalation* pathways are:
  - *Ingestion* of food, water and soil:  
Intake considered to be relatively insignificant.

- *Dermal* absorption:

Primarily from 1,4-dichlorobenzene vapour in the air:

adult - 0.5 to 15 ug/day  
child - 0.2 to 6 ug/day

These ingestion and dermal exposures are generally several times less (although the upper range of dermal exposures overlaps slightly with the lower range of inhalation exposures; see Table 5) than inhalation.

6) These intakes (ie. ingestion and dermal) also overlap with intakes associated with cancer risk from oral exposures (ie. not shown in Table 6 but see Table 1 - 'Allowable' intakes, associated with oral cancer potency factor under Ingestion Guidelines). Although dermal exposures are less than exposures via inhalation, they could be significant in view of the lipophilic nature of the substance. Therefore, in some cases, dermal exposure (ie. this route is the primary contributor to these intakes) may add to the cancer risks (ie.  $\approx 7 \times 10^{-6}$  based on the 15 ug/day maximum dermal value) from exposure to 1,4-dichlorobenzene.

#### Regulatory compliance messages:

- 7) The risk characterization in Table 6 indicates that, for the inhalation receptor exposures considered:
  - The exposures potentially associated with outdoor air quality, for adults, youth and children, fall below the air quality guidelines of various jurisdictions.
  - Exposures associated with typical outdoor exposure (ie. 3 hr) also fall below the air quality guidelines of various jurisdictions
  - Exposures associated with personal activity patterns fall in the lower 1% range of the air quality guidelines of various jurisdictions.

It should be noted that these air quality guidelines may be of different types. Some are purely health based and some are regulatory and therefore may have been influenced by various risk management considerations. The regulatory guidelines may also have different uses (eg. judging the acceptability of air quality per se or judging the incremental addition by a source to the existing air quality).

8) Table 6 also indicates that all the inhalation exposures are less than the available occupational levels (Table 6 indicates that the intake associated with available occupational levels is at 9020000 ug/day).



9) The intakes associated with ingestion and dermal exposures (ie. in Table 5) overlap slightly with the low end of available ingestion guidelines (ie. range 7.5 - 112.5 ug/day in Table 1).

10) MOEE will consider 1,4-dichlorobenzene as a candidate for standard setting.

#### Summary and recommendations:

♦ All the inhalation exposures are less than the range of available chronic acceptable exposure levels and therefore, the possibility of long-term health effects, other than cancer risk, is unlikely.

♦ The range of estimated inhalation risks associated with 'outdoor air quality' (ie. 100% outdoor exposure) is between  $7.4 \times 10^{-6}$  and  $3.6 \times 10^{-5}$ . Similarly the range of risks associated with 'typical personal exposures' is between  $9.8 \times 10^{-6}$  and  $6.2 \times 10^{-4}$ . These risk estimates should be considered provisional since they are based on oral gavage studies, which were used to calculate inhalation cancer potency factors. Since the levels of risk exceed  $1 \times 10^{-5}$ , a level generally deemed to be negligible, it is recommended that 1,4-dichlorobenzene be examined as a candidate for reduction of exposure but in the light of the provisional nature of these risk estimates.

♦ Exposures and therefore risks associated with 'typical personal exposures' (ie. based on surrogate indoor values from three non-Windsor specific studies) are higher than the risks associated with 'outdoor air quality'.

♦ Indoor environments, likely influenced by the use of 1,4-dichlorobenzene as a moth repellent and air deodorant, are the most dominant in the upper range of 'typical personal exposures'.

♦ Ingestion exposures are considered to be relatively insignificant.

♦ Although dermal exposures are less than exposures via inhalation, they could be significant in view of the lipophilic nature of the substance. Therefore, in some cases, dermal exposure may add to the cancer risks (ie. a risk of  $\approx 7 \times 10^{-6}$  based on the 15 ug/day maximum dermal value) from exposure to 1,4-dichlorobenzene.

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## APPENDIX 6

### RISK ANALYSIS FOR CADMIUM





APPENDIX 6  
RISK ANALYSIS FOR CADMIUM

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## CADMIUM

### DESCRIPTION and SOURCES of CADMIUM.

Cadmium (Cd), a naturally occurring element present in the earth's crust, is a soft, silver-white metalloid. This form, however, is not common in the environment. Rather, cadmium is most often encountered in combination with other elements such as oxygen (cadmium oxide), chlorine (cadmium chloride), or sulfur (cadmium sulfide). These compounds are all stable solids that do not evaporate, although cadmium oxide is often found adsorbed to small particulates present in air.

Cadmium is released as a by-product during the processing of zinc-bearing ores, and also from the smelting of lead and copper ores. Major uses include metal plating, pigments, nickel-cadmium batteries and plastic stabilizers.

Cadmium enters the environment to a limited extent from the natural weathering of minerals, but to a much greater degree from pollutant sources such as discarded metal-containing products and fuel combustion. Significant sources of atmospheric cadmium are fossil fuel combustion (*i.e.*, coal and residential burning of oil and petroleum products). Other significant sources include the smelting of copper, lead, zinc and cadmium, the incineration of municipal waste and sewage treatment sludges, and the iron and steel industry. A major exposure route in humans is inhalation of cigarette smoke.

### 1. HAZARD IDENTIFICATION

An extensive review on the toxicology, human epidemiology, environmental fate, and properties of cadmium was published recently by the Agency for Toxic Substance and Disease Registry (ATSDR) of the US Department of Health and Human Services, Public Health Service<sup>1</sup>. The review, which encompasses past and recent findings obtained from a detailed literature search, provides an excellent integrative and interpretative evaluation of the cadmium issue as related to its potential health effects on humans following exposure through various environmental pathways. As it is the scope of the current document to provide a general, although comprehensive updated overview on the toxicology of cadmium, excerpts of the recent ATSDR document were used in the following sections to summarize the information considered to be of relevance for the Windsor study. A more detailed discussion of the health effects of cadmium may be obtained by consulting the references contained in section 5.

#### 1.1 Absorption and Metabolism

Cadmium in air is present as small particles of CdO, although other salts are possible. Overall absorption depends on the particle size and solubility. About 5-20% (based on animal data) of the inhaled cadmium is retained and absorbed in the alveoli of the lungs. Since no empirical data on cadmium absorption in humans is available, estimates based on models suggest 7 to 50%. Because cigarette smoke has smaller particle sizes, the absorption from it is estimated to range from 27 to 54%<sup>2</sup>.

The absorption in the gastrointestinal tract depends on factors like age, body stores of other metals (iron deficiency results in greater absorption) and the composition of the diet, which may influence the binding and, hence, the absorption of cadmium. About 3-7% of ingested cadmium is absorbed<sup>2</sup>.

Wester *et al*<sup>3</sup> have shown experimentally, using monkeys, that an applied dose of 0.05 % of Cd in water and 0.05% in soil will diffuse through the skin into the plasma in about 16 hours. Cadmium that is retained in the skin will continue diffusing into the plasma.

There is no direct metabolic conversion of the absorbed cadmium, which binds to anionic groups, such

as sulfhydryl groups in proteins, especially to metallothionein (MT), (up to 7 atoms per molecule). Metallothionein is a low molecular weight protein rich in cysteine, whose synthesis can be induced in most tissues, especially in the liver and kidneys, by metals and organic compounds. The binding of cadmium to metallothionein greatly reduces the toxicity of the metal, and also acts as a carrier between tissues, a phenomenon observed in the translocation of cadmium from the liver to the kidneys following acute exposure. Most of the body burden of cadmium under low level and long term exposure is present in the kidneys (up to 1/2) and the liver (1/6), two organs especially rich in metallothionein. The muscles contain about 1/5th<sup>2</sup>.

Most of the ingested or inhaled cadmium is excreted in the feces, since absorption from the gastrointestinal tract is low, and since approximately 60% of the inhaled cadmium is subsequently cleared and swallowed. Further, biliary excretion and excretion across the mucosa of the intestines also occurs. Any absorbed cadmium is excreted slowly, about 50:50 in urine and feces. As a result, the cadmium content of the liver increases to age 20-25, and thereafter remains roughly constant. In the kidney, the maximum concentration is not reached until 40-50 years.

The placenta appears to act as a partial barrier to fetal exposure, since the concentration in the cord is about 1/2 of that in the maternal blood. The cadmium concentration in human milk is only 5-10% of the concentration in the blood.

## 1.2 Toxicology

Toxic effects from the inhalation of cadmium have been observed following occupational exposures to fumes and dust, chiefly to cadmium oxide (CdO). Different cadmium compounds appear to have similar effects when inhaled.

Cadmium dusts and fumes are intensely irritating at high concentrations, and may lead to chronic irritation and/or necrosis of the upper respiratory tract membranes following long term exposure at low concentrations. However, the kidneys are considered as the main target organ following long-term exposure, both from the inhalation and ingestion routes. Abnormal renal function is evidenced by proteinuria (abnormal presence of lower molecular weight proteins in the urine) and decrease in the glomerular filtration rate. It is believed that these effects are caused by cadmium no longer bound to metallothionein. More specifically, the Cd-MT complex which is released from the liver into the systemic circulation, is filtered by the kidney glomerule, taken up in the renal tubules, and rapidly degraded in the phagolysosomes with the release of unbound cadmium<sup>4</sup>. It is believed that protective mechanisms rapidly immobilize the unbound cadmium, thus preventing its interaction with critical cellular sites. However, after a (critical) threshold concentration of approximately 200 ug Cd/g wet weight is attained, these protective mechanisms are no longer sufficient and nephropathies such as proteinuria are observed. Cessation of exposure does not lead to a decrease in proteinuria since cadmium is eliminated very slowly from the body, with an estimated half-life of 15-25 years.

Bone disorders, such as osteoporosis, and the outbreak of the so-called Itai-Itai disease reported in Japanese subjects<sup>2</sup> can be caused by chronic cadmium poisoning through ingestion of contaminated water and food. These, however, appear to be secondary effects from the disruption in the kidney's vitamin D metabolism resulting in an imbalance in calcium absorption and excretion. Other important effects which have been associated with chronic cadmium exposure in humans are hypertension (secondary to nephropathies or as a direct effect of cadmium on blood vessels), and lung fibrosis.

The epidemiological evidence that the inhalation of cadmium compounds in occupational settings (e.g., smelters, manufacture of nickel-cadmium batteries) causes lung cancer in humans is weak and conflicting because of confounding factors such as simultaneous exposure to other metals and smoking. Some

evidence exists for increased mortality from cancer of the pancreas. On the other hand, studies with rats exposed to cadmium chloride ( $\text{CdCl}_2$ ) have demonstrated a dose related increase in primary lung tumors, but no tumors occurring at any other site. No such effects were found in hamsters, and only a weak relationship was observed in mice. In addition, significant injection site-sarcomas and testicular tumors have been found in mice and rats acutely administered with cadmium salts<sup>5</sup>. There is no evidence that ingested cadmium causes cancers in humans, but the statistical power of the studies available is low. No increase in overall cancer incidence, or incidence of a specific tumor type was found in studies with mice or rats.

Based on an extensive review of the literature, the US EPA<sup>6</sup> has classified cadmium as a B1 (probable) carcinogen in humans by the inhalation route. The evidence for carcinogenicity by any other route is considered insufficient. The International Agency for Research on Cancer (IARC)<sup>7</sup> classifies cadmium as a group 2A substance (at least limited evidence of carcinogenicity in humans and sufficient evidence from animal studies).

These classifications are partly supported by the genotoxicity database on cadmium. Indeed, cadmium is a recognized clastogen, inducing mainly single-strand breaks in test systems<sup>8</sup>. On the other hand, mutagenicity tests in bacteria and yeast have been inconclusive, but positive responses have been obtained in mutation assays in Chinese hamster cells and mouse lymphoma cells. Conflicting results have been obtained in assays of chromosomal aberrations in human lymphocytes *in vitro*, or obtained from exposed workers<sup>1</sup>. Several of the positive results have been observed at concentrations in which some cytotoxicity was apparent, suggesting the possibility that the mutagenic effect of cadmium is a non-specific consequence of cell damages<sup>5</sup>.

## 2. DOSE-RESPONSE INFORMATION/CURRENT EXPOSURE GUIDELINES

The uncertainties surrounding the potential toxicological effects of environmental cadmium on communities have influenced the methodologies used to set guidelines and permissible exposure levels. As noted previously, the adoption of reasonably conservative assumptions is warranted in this context in order to provide sufficient protection of public health. This section summarizes various health criteria values, that is, exposure guidelines and dose-response information that leading regulatory agencies (and other relevant sources) have proposed and consider appropriate for permitting, assessing, and characterizing risks associated with various exposures. Potential exposures to cadmium experienced by populations residing in the Windsor airshed are evaluated in section 3 and the risk characterization is presented in section 4.

### 2.1 Air Guidelines

#### 2.1.1 Chronic, Non-Carcinogenic Health Effects

The US EPA's Integrated Risk Information System database<sup>1</sup> notes that the inhalation Reference Concentration (RfC) for cadmium is under review. EPA defines an RfC as an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime.

The California Department of Health Services, as reported in the California Air Toxics "Hot Spots" Program, Risk Assessment Guidelines<sup>9</sup>, has proposed for cadmium an inhalation chronic AEL (Acceptable Exposure Level) of  $3.5 \text{ ug}/\text{m}^3$ . The AEL is used for the evaluation of the potential noncancer adverse health effects of long-term (chronic) exposures. It should be noted, however, that the California AEL was calculated based on the US EPA RfD for cadmium in food ( $10^{-3} \text{ mg Cd/kg-day}$ ) by assuming that an individual weighs 70 kg and breathes  $20 \text{ m}^3$  of air *per day*. As the RfD was set to protect individuals



from kidney effects, this approach may not be appropriate in the case of airborne cadmium in view of the pulmonary (portal-of-entry) effects that may result (e.g., emphysema) following chronic, low level exposure to cadmium compounds<sup>10,11</sup>. This value, therefore, must be considered provisional until the results of the review underway at the US EPA will be made available.

The Massachusetts Department of Environmental Protection<sup>12</sup> has proposed in 1990 a Threshold Effects Exposure Limit (TEL) of 0.0027  $\mu\text{g}/\text{m}^3$ , based on the ACGIH occupational exposure guideline.

The World Health Organization, in its Air Quality Guidelines for Europe<sup>16</sup>, has recommended ambient air guidelines to prevent non-carcinogenic effects following exposure to airborne cadmium that may be present in both rural ( $< 1.5 \text{ ng}/\text{m}^3$ ) and urban ( $10\text{--}20 \text{ ng}/\text{m}^3$ ) areas.

Finally, the Ontario Ministry of the Environment has proposed, in 1974, an Ambient Air Quality Criteria (AAQC) of 2  $\mu\text{g}/\text{m}^3$ . This value, which was taken as being 1/100th of the TLV for dust, was set to prevent bioaccumulation of cadmium and the ensuing nephrotoxicity.

Generally, the inhalation chronic AEL, TEL, AAQC, and the inhalation RfC noted above are comparable in their use for assessing chronic effects (except carcinogenic effects) due to inhalation. It is expected that constraining environmental exposures of human populations to cancer-preventive levels of cadmium should decrease to negligible levels, or simply eliminate depending on the end-point of concern, the probability of occurrence of chronic non-cancer health effects.

## 2.1.2 Carcinogenic effects

For the purpose of estimating cancer risk, the U.S. EPA<sup>6</sup> has established an inhalation unit risk of  $1.8 \times 10^{-3} (\text{ug}/\text{m}^3)^{-1}$  for continuous lifetime exposure to 1  $\text{ug}/\text{m}^3$  of cadmium. In other words, an estimated excess lifetime risk of  $1/10^6$  of contracting cancer in this particular case would be associated with a lifetime average daily exposure (LADE) to  $5.6 \times 10^{-4} \text{ ug}/\text{m}^3$ . This value was derived based on results obtained from a cohort, occupationally exposed to cadmium chloride, which showed a two-fold increase in lung, trachea, and bronchus cancers. Although inhalation studies in experimental animals have demonstrated the carcinogenic potential of cadmium, the US EPA elected to use the human database, despite some shortcomings, in order to minimize uncertainties associated with interspecies extrapolation.

Similarly, the unit risk factor used by the Massachusetts Department of Environmental Protection<sup>12</sup> for total airborne cadmium was  $1.8 \times 10^{-3} (\text{ug}/\text{m}^3)^{-1}$ , resulting in an Allowable Ambient Limit (AEL) of  $1 \times 10^{-3} \text{ ug}/\text{m}^3$  for a lifetime excess cancer risk of  $1/10^6$ . On the other hand, the New York State Department of Health (NYSDOH), as reported in the recent Air Guide-1 published by the New York State Department of Environmental Conservation (NYSDEC)<sup>14</sup>, proposes several unit risk factors for the various forms of cadmium that may be present in the atmosphere. However, for the current study, the unit risk retained was that for total cadmium which is similar to that proposed by the US EPA ( $2 \times 10^{-3} (\text{ug}/\text{m}^3)^{-1}$ ).

Other US states<sup>15</sup>, such as Florida, Kansas, Rhode Island, and Vermont have adopted the US EPA inhalation unit risk factor for the implementation of an annual-based value corresponding to an excess lifetime cancer risk of  $1/10^6$  ( $5.6\text{--}6 \times 10^{-4} \text{ ug}/\text{m}^3$ ), although in some cases (e.g., North Carolina) the annual value was established based on an excess risk of  $1/10^5$ . Substantially higher annual acceptable ambient air concentrations than those obtained with the above mentioned unit risk factors have been proposed by the states of Montana ( $0.07 \text{ ug}/\text{m}^3$ ) and Pennsylvania ( $0.12 \text{ ug}/\text{m}^3$ ). Finally, the California Office of Environmental Health Hazard, Reproductive and Cancer Hazard Assessment Section, as reported in the 1992 California Air Toxics "Hot Spots" Program, Risk Assessment Guidelines<sup>9</sup>, calculated a unit risk factor of  $4.2 \times 10^{-3} (\text{ug}/\text{m}^3)^{-1}$  for cadmium and cadmium compounds, thus resulting in an acceptable ambient air concentration of  $2.4 \times 10^{-4} \text{ ug}/\text{m}^3$  at the  $1/10^6$  risk level.

No air guidelines to prevent potential carcinogenic effects from environmental cadmium have been suggested by the World Health Organization<sup>16</sup> and its affiliated International Agency for Research on Cancer (IARC), although the probable carcinogenicity in humans has been recognized<sup>7</sup>.

Occupational exposure guidelines are available for cadmium. In the US, the American Conference of Governmental Industrial Hygienists (ACGIH)<sup>17</sup> presently has a Threshold Limit Value-Time Weighted Average (TLV-TWA) of 50  $\mu\text{g}/\text{m}^3$  for both dusts and salts (as cadmium), and cadmium oxide fumes (as cadmium). It should be noted, however, that this value was recommended to prevent proteinuria, pulmonary edema, and emphysema. Consequently, as a result of the carcinogenic potential of cadmium, an A2 designation (suspected human carcinogen), and a TLV-TWA of 10  $\mu\text{g}/\text{m}^3$ , as cadmium, was proposed by the TLV Committee and placed on the Notice of Intended Changes.

The Permissible Exposure Limit (PEL-TWA), established by the Occupational Safety and Health Administration (OSHA)<sup>17</sup> is 100  $\mu\text{g}/\text{m}^3$  (TWA), and 200  $\mu\text{g}/\text{m}^3$  for cadmium dusts. These limits were promulgated by OSHA for toxic effects other than cancer.

In 1989<sup>1</sup>, the World Health Organization has recommended a health-based long-term occupational exposure limit of 10  $\mu\text{g}/\text{m}^3$ .

The current Ontario occupational guideline for cadmium is 50  $\mu\text{g}/\text{m}^3$  with a notice of intended change<sup>18</sup> to 20  $\mu\text{g}/\text{m}^3$ .

The above guidelines for atmospheric cadmium are summarized in Table 1 below.

## 2.2 Other Route Guidelines

No quantitative estimates of carcinogenic risk from oral exposure (*i.e.*, cancer potency factor) is proposed by the US EPA<sup>1,6</sup> in view of the lack of evidence of the carcinogenicity of cadmium compounds administered orally to experimental animals, and the lack of availability of human studies. Similarly, no such numbers are available from other jurisdictions and regulatory agencies.

However, because ingestion of contaminated water and food is considered the most important route of exposure to cadmium for the general population, and because several systemic effects other than cancer may be induced following long-term exposure, various standards and guidelines have been proposed in order to regulate the daily intake of this element. Indeed, the EPA<sup>6</sup> recommends two different Reference Doses (RfD) for both food ( $1 \times 10^{-3}$  mg/kg-day) and drinking water ( $5 \times 10^{-4}$  mg/kg-day). These values were obtained by modelling (with a toxicokinetic model) the daily intake of cadmium that would result in a critical concentration of cadmium  $> 200 \mu\text{g Cd/g}$  wet weight in the renal cortex. As noted previously in section 1.2, at these cadmium concentrations severe and irreversible nephropathies occur. The difference in the reported RfDs allows for variations in the fraction of the ingested cadmium through food and drinking water. It should also be noted that these values are individually calculated as a total daily intake with no consideration for relative source contribution. Consequently, the US EPA has proposed a Maximum Contaminant Level (MCL) under the Safe Drinking Water Act (SDWA) of 5  $\mu\text{g}/\text{L}$  which attributes a 25% contribution to intake through drinking water<sup>6</sup>.

TABLE 1. Summary of Exposure Guidelines for Cadmium from Leading Agencies

GUIDELINE APPLICATION	AGENCY(IES)	ORIGINAL VALUE	CONCENTRATION ("Original Form" converted to these as applicable)			CALCULATED "ALLOWABLE" INTAKE (3)
			Unit Risk (1)	RsC (2) (1 x 10 <sup>-5</sup> )	RsC (2) (1 x 10 <sup>-4</sup> )	
INHALATION GUIDELINES						
Occupational	OSHA, ACGIH, OMOL, WHO	10 - 200 ug/m <sup>3</sup>	NA	NA	NA	200000 - 4000000 (0.003 - 0.06)
Ambient Air Quality Guidelines	US states,	5.6 x 10 <sup>-4</sup> - 0.12 ug/m <sup>3</sup>	NA	NA	NA	11 - 2400 (1.6 x 10 <sup>-7</sup> - 3.4 x 10 <sup>-5</sup> )
Ontario Air Quality Guideline	OMOE	2 ug/m <sup>3</sup>	NA	NA	NA	40000 (5.7 x 10 <sup>-4</sup> )
Chronic AELs/RfCs	CDHS, MDEP, WHO	0.0027 - 3.5 ug/m <sup>3</sup>	NA	NA	NA	54 - 70000 (7.7 x 10 <sup>-7</sup> - 1 x 10 <sup>-3</sup> )
Inhalation Cancer Potency Factor	US EPA CARB	See Unit Risk column	1.8 x 10 <sup>-3</sup> 4.2 x 10 <sup>-3</sup>	0.0056 0.0024	0.00056 0.00024	for 1 x 10 <sup>-5</sup> risk: 48 - 112 (6.8 x 10 <sup>-7</sup> - 1.6 x 10 <sup>-4</sup> ) for 1 x 10 <sup>-6</sup> risk: 4.8 - 11.2 (6.8 x 10 <sup>-8</sup> - 1.6 x 10 <sup>-5</sup> )
INGESTION GUIDELINES						
Oral Reference Dose (RfD)	US EPA: Food Drinking Water	0.001 mg/kg-day 0.0005 mg/kg-day	-	-	-	70000 35000
Drinking Water Guideline	HWC, US EPA, US states	5 - 10 ug/L	-	-	-	7500 - 15000 (1.1 x 10 <sup>-6</sup> - 2.1 x 10 <sup>-4</sup> )
Oral Cancer Potency Factor	NA	-	-	-	-	-

<sup>1</sup>For inhalation and ingestion guidelines, unit risks are expressed as (ug/m<sup>3</sup>)<sup>-1</sup> and (ug/L)<sup>-1</sup>, respectively

<sup>2</sup>For inhalation and ingestion guidelines, risk specific concentrations are expressed as ug/m<sup>3</sup> and ug/L, respectively

<sup>3</sup>Intake was computed by assuming, where applicable, an adult weight of 70 kg, a breathing rate of 20 m<sup>3</sup>/day, a water intake of 1.5 L/day. In all cases 100% bioavailability of the intake was assumed.

Similarly, the Canadian drinking water objective, which was based on the conclusions of a joint FAO/WHO expert committee, estimated a provisional tolerable weekly intake of 0.4-0.5 mg Cd. Since food is the main source of cadmium for people not occupationally exposed, and since it would be difficult to reduce cadmium intake from food, it was recommended that the intake from water should be kept as low as possible. A maximum concentration of 5 ug/L in drinking water combined with a consumption of 1.5 L/d was proposed. This would result in the ingestion of about 12% of the provisional tolerable intake. The maximum acceptable concentration therefore is 5 ug/L<sup>19</sup>.

Other US states have similar drinking water quality standards, ranging from 5 ug/L (Vermont, Maine, Kansas) to 10 ug/L (Alabama, Arizona, Massachusetts, Minnesota, Rhode Island).

The above guidelines are summarized in Table 1.

### 3. HUMAN EXPOSURE ASSESSMENT

#### 3.1 Inhalation

##### 3.1.1 Ambient Air Quality

Ambient levels of cadmium have been measured at eleven fixed site stations in Windsor by the Ontario Ministry of Environment and Energy. For this assessment, data from all these sites were available. The measurements include four years of data and 2840 samples, each collected over a 24 hour period. Concentration levels range from non-detectable to 91 ng/m<sup>3</sup>, with the median, mean (average), 90th percentile and 95th percentile levels being 1.0, 1.6, 4.0 and 6.0 ng/m<sup>3</sup>, respectively<sup>20</sup>.

Table 2. Estimated Daily Intakes of Cadmium Associated With Ambient Air Quality in Windsor

Air Quality Measure (a)	Concentration	Adult (b)	Child (b)
	ng/m <sup>3</sup>	ng/day (ng/kg-day)	ng/day (ng/kg-day)
Median	1.0	20 (0.29)	5.0 (0.3)
Mean	1.6	32 (0.46)	8.0 (0.5)
90th percentile	4.0	80 (1.14)	20.0 (1.3)
a) Based on 2840, 24 hour average samples b) Assuming the following weights and inhalation rates per day (ie. per 24 hour period): Adult: 70 kg; 20 m <sup>3</sup> /day Child: 15 kg; 5 m <sup>3</sup> /day			

It is possible to estimate the daily intake of cadmium associated with these measures of Windsor ambient air quality, recognizing that personal real exposures/intakes may be quite different as further discussed in section 3.1.2. Table 2 shows these estimated intakes for two different receptors, i.e., an adult and a child. It should be noted that these intakes were calculated based on 24 hour exposures and assume 100%



bioavailability by the inhalation route.

### 3.1.2 Microenvironments

It is reasonable to assume that the daily cadmium intakes associated with typical personal exposure patterns can be better estimated from various microenvironmental concentrations than from fixed site monitoring data. For the purpose of scoping population exposures, the set of typical receptors in Table 3 below was considered. Examples of the receptor types and/or their characteristics are also included in Table 3. Using cadmium concentrations acquired in various microenvironments, either as part of the personal exposure or subsequent microenvironment study in Windsor, it is possible to scope out various typical personal inhalation exposure scenarios for the above receptors. The estimated daily intakes (in ng/day) of these receptors are summarized in Table 4.

Table 3. Receptors With Typical Personal Exposure Patterns

NAME OF RECEPTOR TYPE	CHARACTERISTICS	NAME OF RECEPTOR TYPE	CHARACTERISTICS
Average Office Worker (Non-smoking)	Eg. - Typical office worker (Based on Windsor volunteers and US EPA TEAM study; not smoking at home)	High Outdoor Receptor	Eg. - Construction workers; - Bicycle couriers - Police - Long distance runners
Average Office Worker (Smoker Environment)	Eg. - Typical office worker (Based on Windsor volunteers and US EPA TEAM study; smoking at home)	High Indoor Receptor	Eg. - 'Shut-ins'- Invalids - Elderly, non-mobile
Average Youth	Eg. Special exposures at shopping malls and athletic facilities (pools) in addition to school;	High Commuting Receptor	Eg.- Bus drivers - Taxi drivers - Delivery/ Distribution Services
Average Child (Non-Smoker Home & No Exposure to Tobacco Smoke)	Eg. Similar to average office worker except 'School' replaces 'Office';	Active Receptor # 1	Eg.- 7 hr/week in Bingo Hall or Bar
Average Child (Non-Smoker Home & Typical Exposure to Tobacco Smoke)	Eg. Includes typical times that children may be in proximity to tobacco smoke, outside the home, based on activity pattern studies;		
Average Child (Smoker Home with Exposure to Tobacco Smoke)	Eg. Child living in a house where there is a smoker		



Table 4. Estimated Daily Intakes (ng/day) Associated with Typical Personal Exposures (See footnote 1.)

MICRO ENVIRONMENT	Air Concentration (ng/m <sup>3</sup> ) (h)	Average Office Worker		Youth	Average Child		High Outdoor Receptor	High Indoor Receptor	High Commuting Receptor
		Non-smoker	Smoker Home Environment		Non smoker home/No exposure to tobacco smoke	Non smoker home/Typical exposure to tobacco smoke			
		Time spent (hrs)	Time spent (hrs)	Time spent (hrs)	Time spent (hrs)	Time spent (hrs)	Time spent (hrs)	Time spent (hrs)	Time spent (hrs)
Office	0.8/2.2 (m)	6.7(a)	6.7(a)				1.7		
School	0.8/2.2 (d)			6.7	6.7	6.7			
Home	0.7/1.4 (m)	13.3(b)		13.3	13.7	12.4	13.7	20.4	13.7
Commuting (in-transit)	1.6/4.0 (n)	1.0(a)	1.0(a)	1.0(f)	1.0(f)	1.0(f)	1(a)	1(a)	7.7
Urban (Outdoors)	1.6/4.0	2.6(a)	2.6(a)	2.6	2.6	2.6	7.6(g)	2.6	2.6
Home with smokers	0.8/1.8 (c)		13.7(b)			1.3(e)			
Shopping Mall/Market	1.5/2.0 (k)	0.4(i)		0.4(i)					
Bar or Bingo Hall	4.1/7.3 (o)								
INTEGRATED EXPOSURE (ng-hrs/m <sup>3</sup> )		21.0/48.6	22.1/53.8	21.0/48.6	20.7/48.3	20.8/48.8	24.7/57.3	20.0/43.0	26.1/60.4

TIME WEIGHTED AVERAGE EXPOSURE (ng/m <sup>3</sup> over 24 hr) (h)	0.9/2.0	0.9/2.2	0.9/2.0	0.9/2.0	0.9/2.0	0.9/2.0	1.0/2.4	0.8/1.8	1.1/2.5
INTAKE/DAY (NG/DAY) (h)	17.5/40.5	18.4/44.8	12.3/ 28.3	4.3/10.1	4.3/10.2	20.6/47.8	16.7/35.8	21.7/50.3	

### Estimations:

- \*  $\text{INTEGRATED EXPOSURE (ng-hrs/m}^3\text{)} = \text{SUM OF}[\text{Microenvironment concentration} \times \text{Time spent in Microenvironment}]$
- \*  $\text{TIME WEIGHTED AVERAGE EXPOSURE (ng/m}^3\text{)} = \text{INTEGRATED EXPOSURE/24 hr}$
- \*  $\text{INTAKE/DAY (ng/day)} = \text{TIME WEIGHTED AVERAGE EXPOSURE} \times \text{DAILY BREATHING RATE (ie. for Adult or Youth or Child as applicable)}$

### Footnotes:

- a.) TIME BUDGET ANALYSIS; Windsor '91 Summer PEP Study; Handout to Volunteers; May/92 (R. Bell)
- b.) Sum of 'Indoor, Home' and 'Indoor Other' in a.)
- c.) Determination of the contribution of tobacco smoke to indoor levels of cadmium is still in the development stage. This value was obtained during the personal exposure study in Windsor from homes where smoking was permitted.
- d.) Assumed to be same 'microenvironment' concentration that were measured by PEP study in the 'Office' environment.
- e.) Average time spent in proximity to tobacco smoke, in various locations outside the home, was approximately 1.3 hours, based on a study of children's activity patterns; (Ref: Study of Children's Activity Patterns; State of California, Air Resources Board, Contract No. A 733-149). Assume that benzene concentrations, when in proximity to tobacco smoke is represented by the median levels referenced in footnote "c," above.
- f.) Assume 1 hour is spent in the car per day.
- g.) For the 'high-outdoor' receptor, urban outdoor concentrations were assumed to be represented by the 'mean' and 90th percentile concentrations taken from the fixed site monitoring network. Also assume that for this group, the 6.7 hours of 'at work' exposure is divided so that 1.7 hours is spent in the office and 5 hours is added to the 2.6 hours of urban outdoor exposure for a total of 7.6 hours.
- h.) First number is the 'mean'. The second number is the 90th percentile, if available; otherwise it is the maximum value measured.
- i.) Assumed that approximately 2.8 hours per week are spent on malls shopping; this was distributed over seven days yielding '0.4 hours/day' in malls.
- j.) Assumed that this receptor spends approximately 7 hours per week in a bingo hall or bar; this was distributed over seven days yielding '1 hr/day' in bingo halls or bars.
- k.) These two values represent the minimum and maximum values in a limited data set.
- l.) Two additional typical personal exposure patterns that were evaluated but are not shown in detail in this table are the 'Average Child in a Smoker Home' and the 'Active Receptor # 1' as noted in Table 3 above. The corresponding intakes/day (ie. mean/90th percentile) for these two receptors are 4.6/11.2 and 20.1/45.2 ng/day, respectively.
- m.) The 'mean' and '90th percentile' concentrations for the 'Office', 'Home' and 'Commuting' microenvironments were derived from the Summer 1991 and Winter 1992 personal exposure studies in Windsor.
- n.) Since no data was available for the 'commuting' environment, levels found in 'outdoor' air was assumed to be representative.
- o.) Limited data from 'bingo halls' were used and assumed to be representative for both of these microenvironments.

In order to place the above inhalation exposures (ie. intakes) in Windsor in perspective, it is appropriate to compare to daily intakes that people who smoke may experience.

### 3.1.3 Smoking.

Guerin *et al* (Ref.21, table 12.7) report that cigarettes contain 0.2-4.0 ug Cd/g, that about 2-10% is transferred to the mainstream smoke (<0.1-0.5 ug/cigarette) and that 0.4-0.7 ug/cigarette are transferred to sidestream smoke. These values are somewhat higher than those reported by Elinder<sup>22</sup>, who reports that 0.1-0.2 ug/cigarette might be inhaled from a cigarette with a Cd content of 1-2 ug; that is, ≈10% is transferred. He also notes that tobacco grown in less developed countries have 10-30% of the Cd content of US cigarettes. A person smoking a pack a day - 25 cigarettes - would inhale between <2.5 to 12.5 ug/d according to Guerin *et al*<sup>21</sup> or 2.5 to 5 according to Elinder<sup>22</sup>; or a range of <2,500 to 12,500 ng/d.

Non-smokers who are heavily exposed to environmental tobacco smoke inhale the equivalent of 1/3 to 3 cigarettes per day or <30 to 1,500 ng of cadmium/day (Blot and Fraumeni<sup>30</sup>). Vainio<sup>32</sup> states that the exposure of non-smokers to environmental tobacco smoke would be about 1% of that of active smokers or 25 to 125 ng/day, whereas Remmer<sup>31</sup> gives as an upper limit the equivalent of only 1/5 of a cigarette per day or about <20 to 100 ng/day. Hiller (1984), quoting other authors, gives intakes ranging from a low of 0.001 cigarette equivalents (CE)/hr or 0.01 CE/day, assuming 12 hr exposure, to a high of 27 CE/day. The higher value is clearly anomalous as the range claimed by the other authors is 0.001 to 0.2 CE/hr. The lower value gives an intake of 10 to 50 ng/day.

Furthermore, it is also important to place the inhalation exposures (ie. intakes) in Windsor into perspective, relative to general exposures from other media (ie. see Section 3.2).

### 3.2 Other Routes

In this section, possible non-inhalation routes of exposure (ie. ingestion and dermal) are assessed.

#### 3.2.1 Ingestion of Food

HWC<sup>23</sup> cites studies of Cd intake from food. The intakes range from 20 to 60 ug/d. A survey of Canadian diets found that the mean intake was approximately 14 ug/d, with a range of 7 to 34 ug/day. Daily intakes in the USA have ranged from 10 to 40 ug/d.

Elinder<sup>24</sup> states that the mean intakes in the USA, most European countries and New Zealand is 10-25 ug/d, based on more recent and reliable estimates. The estimated intakes in different countries tend to become lower in more recent studies, possibly because analytical methods have improved. Large individual variations occur due to different dietary habits and age.

ATSDR (Ref.1, table 5-2) has reported the concentration of Cd in many food types. Combining these concentrations with the amounts of food consumed by adult Canadians, as given in Dabeka *et al* (Ref. 25, table 1) gives an intake of 18.5 ug/d.

Dabeka and McKenzie<sup>26</sup> estimate that the average intake for children 0-1 years is 2.8 ug/d or 0.37 ug/kg/d. This includes the very small intake from water (0.044 ng/g). The strongest influence on the amount of Cd ingested is whether or not soya-based formulas were used, since these formulas contain about twice as much Cd as milk-based formulas.

### 3.2.2 Drinking Water

MOEE monitored the raw and treated water at Windsor 8 times in both 1990 and 1991. All of the samples were below the detection limit of 0.05 ug/L.

A drinking water survey done in 1977/78 by Health and Welfare Canada<sup>27</sup> shows that the average for the 18 and over age group is 1.49 L/d, with 90% of the group consuming <2.59 L/d. The mean for children under 6 years is 0.76 L/d, with 90% of this population consuming <1.5 L/d. The intake covers both tap water drunk directly and tap water based fluids such as coffee, tea, soup etc.

The average intake of Cd from drinking water, using the detection limit concentration, is:

adults:	<0.075 ug/d, with 90% of the adults ingesting	<0.13 ug/d.
children:	<0.04 ug/d, with 90% of the children ingesting	<0.075 ug/d.

### 3.2.3 Soil

The cadmium concentration in the soil shows a distinct decreasing trend with distance in a southeasterly direction away from the Detroit River. The median and 90th percentiles are, in ug/g:

	<u>Median</u>	<u>90th</u>
within Windsor	0.7	1.35
15-25 km from river	0.65	0.9
30 km from river	0.25	0.5
eastern shore of L.St.Clair	<0.2	

The concentrations away from Windsor agree with the values reported by Elinder<sup>22</sup> in Sweden - median concentration 0.22 ug/g - and Japan - 0.3 to 0.4 ug/g.

A reasonable estimate for the amount of ingested soil and dust is 80 mg/d for children and 20 mg/d for adults (MOEE<sup>28</sup>, Appendix 1), although values as low as 0 for children <1 y, 40 mg/d for children 1-6 y and 10 mg/d for persons > 6 y have been used (Sheehan *et al*<sup>29</sup>). Using the MOEE soil ingestion values, the intakes from soil in Windsor (ie. 'within Windsor') are:

adults:	0.014 - 0.027 ug/d
children:	0.056 - 0.11 ug/d

In the countryside, outside of the town, the intakes are:

adults:	0.005 - 0.01 ug/d
children:	0.02 - 0.04 ug/d

There is no information available on the amount of cadmium absorbed from soil in the gastrointestinal tract, but it is unlikely to be more than the 3-7% reported for absorption from food (see s.1.1). The amount



absorbed is then 0.4 - 1.9 ng/d for adults and 1.7 - 8 ng/d for children.

### 3.2.4 Dermal

#### 3.2.4.1 During Showering and Bathing

Wester *et al*<sup>3</sup> have demonstrated experimentally *in vitro*, using human skin, that, after a 30 minute exposure to Cd in water followed by skin surface wash with soap and water and an additional 48 h of perfusion,  $\approx 0.5\%$  of the dose of Cd diffuses into the plasma. The water load on the skin was 5 uL/cm<sup>2</sup>, corresponding to a thin layer of water which covers the skin but does not run off. The calculated thickness of the layer is 0.05 mm. Assuming the same water loading when showering and maximum concentration of 0.05 ug/L (see s.3.2.2) produces a loading of  $2.5 \cdot 10^{-7}$  ug/cm<sup>2</sup>. The median surface area of a child is 0.731 m<sup>2</sup> (US-EPA<sup>13</sup>; table 8-4 for age 4<5 y) and the 90th percentile is 0.821. For an adult, the values are, respectively, 1.94 and 2.28 m<sup>2</sup> (US-EPA<sup>13</sup>; table 8-3). These areas are estimated from models and are not measured directly.

The maximum amounts absorbed during a shower, assuming that 0.5 % is absorbed, are:

adult:	0.02 to 0.03 ng
child	$\approx 0.01$ ng

A shower is assumed to last 15 minutes whereas the experimental exposure lasted 30 minutes. The amount absorbed is therefore probably somewhat less than that calculated above. The amount absorbed during a bath should be close to the calculated amounts.

#### 3.2.4.2 Contact With Soil and Dirt

Wester *et al*<sup>33</sup> have measured the *in vitro* absorption of cadmium from water and soil into human skin. After a 16 hour exposure, the amount found in the human plasma receptor fluid was 0.02-0.07% and in the skin, 0.06-0.13%. Almost all of the applied dose could be removed by washing with soap and water.

The most appropriate daily loading of soil on exposed skin is estimated to be 1.8 mg/cm<sup>2</sup> (range 0.5 - 2.8). The exposed area is taken to be 1580 cm<sup>2</sup> for a child and 1980 for an adult, or basically the hands and arms (Sheehan, P.J. *et al*<sup>29</sup>). It is unlikely that the skin is as contaminated in winter as in summer or that the hands and arms are covered by dust 24 hours a day. Therefore, the amounts absorbed are likely to be less than the amounts calculated below.

Taking the amount absorbed as 0.02-0.07% and, a skin loading of 1.8 mg/cm<sup>2</sup>, the median soil concentration as 0.7 ug/g and the 90th percentile as 1.35 (s.3.2.3), the amount absorbed through the skin is:

adults:	median:	0.5 - 1.7 ng/d
	90th percentile:	1.0 - 3.4 ng/d
children:	median:	0.4 - 1.4 ng/day
	90th percentile:	0.8 - 2.7 ng/d

#### 4. RISK CHARACTERIZATION AND PERSPECTIVES

Exposures, expressed as daily intakes in units of ng/day, were assessed in section 3. Inhalation, ingestion and dermal routes of exposure were considered. Table 5 below summarizes the daily intakes (or ranges of daily intakes) of cadmium, for adults and children, estimated in section 3. It should be noted that in section 3, the intakes for inhalation and sometimes for ingestion assumed 100% bioavailability. The intake for dermal exposures are amounts absorbed systemically and hence already include bioavailability considerations. Table 5 has two columns for both adults and children. The first set of columns (ie. '100 % Bioav') give the intakes with 100 % bioavailability having been assumed; the second set (ie. 'Bioav. Incl.'). gives intakes for which bioavailability has been taken into consideration (ie. if information was available as noted in the footnotes). This second set of columns should give a better picture of the relative importance of various exposure routes. As far as comparison to exposure guidelines and intakes associated with cancer risk, the intakes in the first set of columns of Table 5 will be used since the exposure guidelines are also expressed as intakes for which we have assumed 100 % bioavailability.

To characterize risks, the various exposure guidelines discussed in Section 2 are compared to the estimated exposures from inhalation and other routes as discussed in Section 3. Because of the assumptions, uncertainties and ranges of values available from both exposures (see Table 5) and the various exposure guidelines (see Table 1), risk characterization is most appropriately done by comparison of ranges of values.

Table 6 below provides a graphic representation of this comparison of exposures, exposure guidelines and intakes associated with inhalation cancer risk, based on ng intake/day (ie. 'INTAKE in Nanograms per day' increasing upwards on the vertical scale).

The middle section of Table 6, "Exposures", depicts the exposures calculated in Section 3, expressed as intake/day (ie. ug/day). The exposures depicted are: *Outdoor Air Quality* - the exposure from spending 100 % of the day outdoors; *Typical Outdoor Exposure* - the exposure from three hours only outdoors, provided for perspective on the contribution to risk solely from contaminants present in outdoor air; *Typical Personal Exposures* - the range of exposures associated with ten different exposure scenarios, combining periods of indoor, outdoor and various microenvironment exposures. Exposure scenarios are included for adults and children, assuming 20 and 5 m<sup>3</sup>/day inhalation rates respectively. For 'outdoor air quality' (ie. 100% outdoor exposure), for 'typical outdoor exposures' (ie. 3 hr), and for the 'typical activity patterns' the ranges shown, bracket the lowest mean to the highest 90th percentile. For perspective purposes, the exposures of smokers, directly from smoking activity is also depicted in this section.

The left section of Table 6, "Exposure Guidelines", expresses the various guidelines discussed in Section 2 in terms of calculated "allowable" intake/day for adults and children. The values are taken from Table 1. Within each type of guideline group (eg. outdoor air) ranges of exposure guidelines, when available, are indicated. Thus, ranges of Air Quality Guidelines (ie. 'Outdoor Air'), Occupational guidelines (ie. 'Workplace Air'), and chronic health effects based reference concentrations (ie. 'Chronic AEL') are shown. The existing MOEE guideline for cadmium is also shown as a horizontal bar. Comparison of "Exposure Guidelines" to "Exposures" should be done with care. For example, occupational guidelines are included for perspective purposes only. For caveats regarding this comparison see section 4.1.1 of the main report.

The right section of Table 6, "Intakes Associated With Cancer Risk", shows the intakes associated with different levels of cancer risk. Ranges of carcinogenic risk levels (associated with  $1 \times 10^{-5}$  risk and  $1 \times 10^{-6}$  risk) are depicted. Comparison of "Exposures" to "Intakes Associated With Cancer Risk" is appropriate for adult exposures only, since cancer risk estimates apply to a lifetime of exposure and people are adults for the majority of their lives. Adult exposures in the bars of the "Exposure" section fall in the top 70 % of the bars which represent exposures of adults and children.

Based on the tabular analysis (Table 5) and the graphic risk characterization (Table 6), the following observations and deductions can be made:

#### Health messages:

1) It is apparent, that the ingestion route exceeds all other exposure routes for cadmium. Exposures by inhalation are significant but are considerably less. It should be noted that only about 3-7% of ingested cadmium is absorbed. As shown in Table 5 (ie. in the 'Bioav. Incl' columns), even with this low absorption of cadmium, ingestion still remains the dominant route of exposure for the non-smoker. Dermal exposure appears to be least important route of exposure.

2) All the inhalation exposures associated with typical outdoor exposures (ie. 3 hr) and with personal activity patterns are less than the range of available chronic acceptable exposure levels (ie. 54-70000 ng/day; see Table 1) proposed by CDHS, MDEP and WHO. However, some of the exposures associated outdoor air quality (ie. 100 % outdoor exposure) fall in the lower 1 % range of these chronic acceptable exposure levels. These chronic acceptable exposure levels are considered to be purely health based and are protective against all chronic health effects other than cancer risk. Therefore, there is a possibility of long-term health effects associated with outdoor air quality (ie. 100 % outdoor exposure).

This comparison of exposures to chronic acceptable exposure levels can also be expressed more quantitatively in the form of a hazard index. These hazard index comparisons for all substances are summarized and are found in section 4.1.5 of the main report.

3) The most conservative range of available exposure guidelines are depicted in Table 6 under Intakes Associated with Cancer Risk. These guidelines were proposed by CDHS, the US EPA, and the New York State Department of Health (NYSDOH). As shown in Table 6, they overlap with the estimated exposures. Because people are adults for the majority of their lives, these intakes associated with cancer risk are depicted for adults only. The inhalation intakes for adults associated with 'outdoor air quality' (ie. 100 % outdoor exposure), 'typical outdoor exposure' (ie. 3 hr) and 'typical personal exposures' range between 32 - 80 ng/day, 4 - 10 ng/day and 17.5 - 50.3 ng/day, respectively (from Tables 2, 4 and 5). These intakes and the corresponding doses in mg/kg-day are summarized in Table 7. Using the various potencies from the three agencies, the range of risks associated with 'outdoor air quality' (ie. 100% outdoor exposure) is between  $2.9 \times 10^{-6}$  and  $1.7 \times 10^{-5}$ . Similarly the range of risks associated with 'typical outdoor exposures' (ie. 3 hr) is between  $3.6 \times 10^{-7}$  and  $2.1 \times 10^{-6}$ . Similarly the range of risks associated with 'typical personal exposures' is between  $1.1 \times 10^{-6}$  and  $1.1 \times 10^{-5}$ . The risks associated with 'typical personal exposures' and the risks associated with 'outdoor air quality' are very similar and are slightly higher than the risks associated with 'typical outdoor exposures'. This range of risk analysis is summarized in Table 7. It should be further noted, that this risk characterization (ie. using carcinogenic risk based limits) is based on an assumed lifetime exposure (ie, 24 hours, every day, for 70 years) and hence is a very conservative assumption.

4) The exposure that a smoker experiences is considerably higher than any of the exposures associated with 'personal activity patterns', 'outdoor air quality' and 'typical outdoor exposures'.

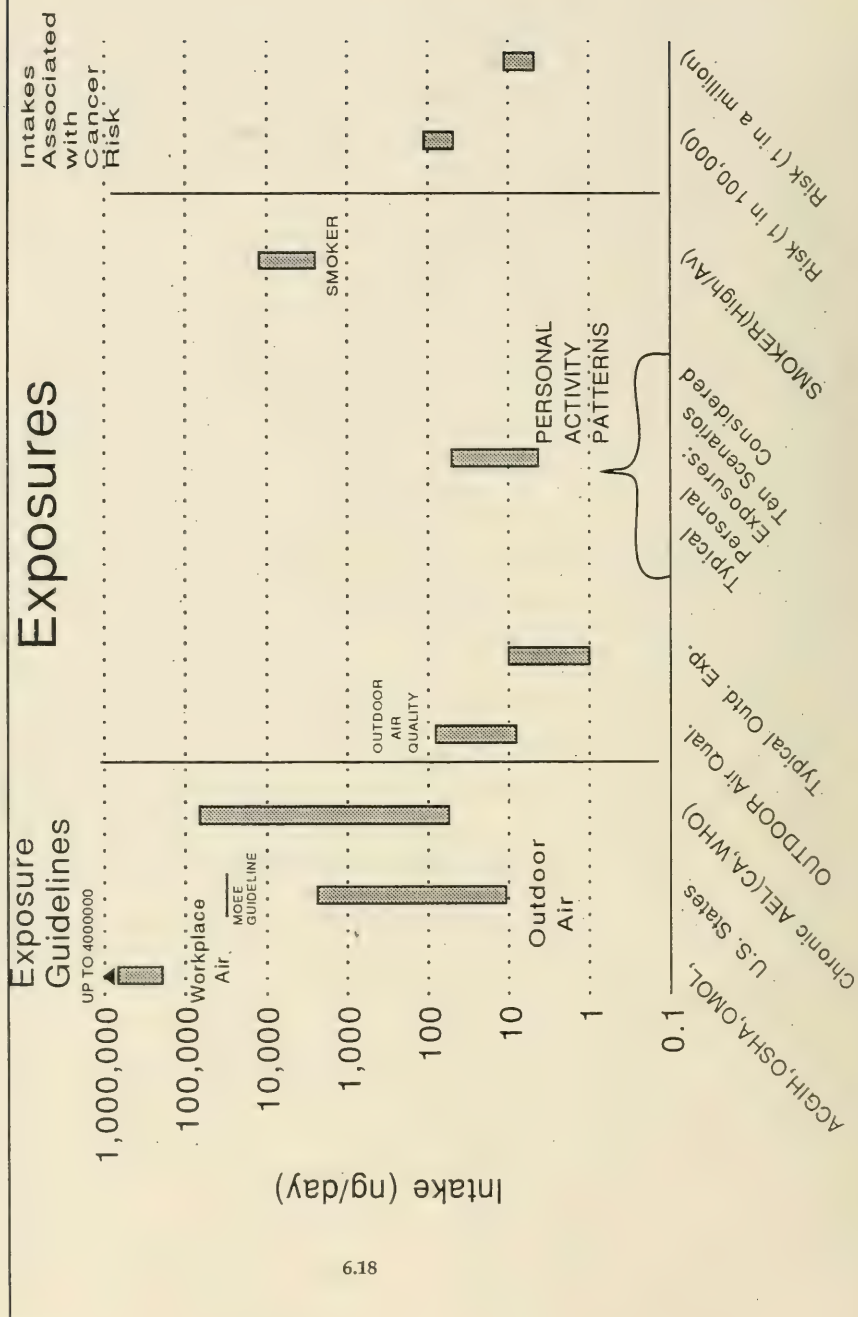
5) For a smoker, the inhalation exposure is dominated by the cadmium in cigarettes.



Table 5. Summary of Estimated Daily Intakes and/or Range of Intakes (in ng /day), from Various Exposure Pathways (ie. intakes, assuming 100 % bioavailability and intakes with bioavailability taken into consideration)

EXPOSURE PATHWAY		ADULT ng/day  (100 % Bioav.)	ADULT ng/day  (Bioav. Incl.)	CHILD ng/day  (100 % Bioav.)	CHILD ng/day  (Bioav. Incl.)
INHALATION	Outdoor Air Quality - Windsor (ie. 100 % outdoor exposure)(a)	32 - 80	16 - 40 (f)	8 - 20	4 - 10 (f)
	Typical outdoor exposure (ie. $\approx$ 3hr)(b)	4 - 10	2 - 5 (f)	1 - 2.5	0.5 - 1.3 (f)
	Typical personal exposures(ie. Table 4) (c)	17.5 - 50.3	8.8 - 25.2 (f)	4.3 - 11.2	2.2 - 5.6 (f)
	Smoking (e)	<2500 - 12500	<1000 - 5000 (e)		
INGESTION	Food (d)	18500	560 - 1300	18500	560 - 1300
	Drinking water (d)	<130	<4 - <9	<75	<2 - <5
	Soil (g)	14 - 27	0.4 - 1.9	56 - 110	1.7 - 7.7
	TOTAL (Ingestion)	$\approx$ 18650	564 - 1310	18630 - 18685	564 - 1310
DERMAL	During showering		0.02 - 0.03		$\approx$ 0.01
	Contact with soil & dirt		0.5 - 3.4		0.4 - 2.7
	TOTAL (Dermal)		0.5 - 3.4		0.4 - 2.7
<p>a.) Range of intakes is associated with the range of the 'mean' to '90th percentile' concentrations in outdoor air. It is to be noted that people are not exposed 24 hours to outdoor air. This estimation assumes 100 % exposure to outdoor air and is a measure of outdoor air quality per se and not of actual exposure.</p> <p>b.) Range of intakes calculated from the 'mean' to '90th percentile' concentrations in outdoor air and assuming a 'typical' outdoor air exposure of <math>\approx</math> 3 hr(ie. corresponding to breathing 2.5 m<sup>3</sup>/3hr for adults and 0.63 m<sup>3</sup>/3hr for children.</p> <p>c.) Range of intakes is estimated from the range of the lowest 'mean' and the highest '90th percentile' concentrations obtained from personal exposure and microenvironment measurements.</p> <p>d.) About 3 - 7 % of ingested cadmium in food and water is absorbed (s. 1.1). The intakes of children and adults are assumed to be the same.</p> <p>e.) The intake shown is the direct intake (ie. from average to upper bound estimate) of an adult smoker from smoking activity (ie. 'smoking') only. Various smoking environments for adults and children have already been included in the 'typical personal exposure' scenarios. The absorption of cigarette smoke is estimated to range from 27 to 54 % of the amount inhaled. The average is <math>\approx</math> 40 % (s. 1.1).</p> <p>f.) An absorption rate of 50% was selected from the available data (see s 1.1).</p> <p>g.) There is no information on the amount absorbed from cadmium on soil. It is assumed that 3 - 7 % (ie. same as for food and water) is absorbed (s 3.2.3).</p>					

Table 6. CADMIUM RISK CHARACTERIZATION in WINDSOR  
 Ranges of exposure guidelines, exposures and risk estimates  
 (Inhalation unless otherwise specified)





6) Considering the information in Table 5, the exposures from the *non-inhalation* pathways are:

- *Ingestion* of food, water and soil:

adult -  $\approx$  18650 ng/day ('100 % Bioav.' column)  
564 - 1310 ng/day ('Bioav. incl.')

child - 18630 - 18685 ng/day ('100 % Bioav.' column)  
564 - 1310 ng/day ('Bioav. incl.')

- *Dermal* absorption:

During showering and bathing and from soil and dirt: around 0.4 to 3.4 ng/day

As noted before, these combined ingestion (both with and without bioavailability considerations) and dermal exposures exceed inhalation exposures. However, in view of the lack of evidence of the carcinogenicity of cadmium compounds administered orally to experimental animals and the lack of availability of human studies, it is unlikely that these exposures will add to the cancer risk from exposure to ingested cadmium.

Table 7. Range of Inhalation Cancer Risks Associated with Estimated Intakes (ie. for adult exposures only) of Cadmium

RANGE of INHALATION INTAKES			POTENCY (a)		RANGE of RISKS
Environment	Unit ng/day	Unit mg/kg/day	Agency	Unit (mg/kg-d) <sup>1</sup>	
OUTDOOR AIR QUALITY (Windsor)	32 - 80	4.6 x 10 <sup>-7</sup> - 1.1 x 10 <sup>-6</sup>	EPA	6.4	2.9 x 10 <sup>-4</sup> - 7.0 x 10 <sup>-4</sup>
			CDHS	15.0	6.9 x 10 <sup>-4</sup> - 1.7 x 10 <sup>-3</sup>
			NYSDOH	7.1	3.3 x 10 <sup>-4</sup> - 7.8 x 10 <sup>-4</sup>
			OVERALL RANGE OF RISKS: 2.9 x 10 <sup>-4</sup> - 1.7 x 10 <sup>-3</sup>		
TYPICAL OUTDOOR EXPOSURE (ie.= 3 hr.)	4 - 10	5.7 x 10 <sup>-8</sup> - 1.4 x 10 <sup>-7</sup>	EPA	6.4	3.6 x 10 <sup>-7</sup> - 9.0 x 10 <sup>-7</sup>
			CDHS	15.0	8.6 x 10 <sup>-7</sup> - 2.1 x 10 <sup>-6</sup>
			NYSDOH	7.1	4.0 x 10 <sup>-7</sup> - 9.9 x 10 <sup>-7</sup>
			OVERALL RANGE OF RISKS: 3.6 x 10 <sup>-7</sup> - 2.1 x 10 <sup>-6</sup>		
TYPICAL PERSONAL EXPOSURES	17.5 - 50.3	2.5 x 10 <sup>-7</sup> - 7.2 x 10 <sup>-7</sup>	EPA	6.4	1.6 x 10 <sup>-4</sup> - 4.6 x 10 <sup>-4</sup>
			CDHS	15.0	3.8 x 10 <sup>-4</sup> - 1.1 x 10 <sup>-3</sup>
			NYSDOH	7.1	1.8 x 10 <sup>-4</sup> - 5.1 x 10 <sup>-4</sup>
			OVERALL RANGE OF RISKS: 1.6 x 10 <sup>-4</sup> - 1.1 x 10 <sup>-3</sup>		
a. These are equivalent potency factors calculated from the unit risks proposed by the agencies listed; assumed adult weight of 70 kg and 20 m <sup>3</sup> per day.					

7) The amount of cadmium that may be ingested from food (ie. 18500 ng/day from Table 5) and from drinking water (ie. range of <75 - <130 ng/day from Table 5) are less than the corresponding U.S. EPA oral RfDs (ie. 0.001 mg/kg-day and 0.0005 mg/kg-day respectively) corresponding to 'allowable' intakes of 70000 and 35000 ng/day (ie. see Table 1) respectively. These oral RfDs were set to prevent systemic, non-carcinogenic effects.

#### Regulatory compliance messages:

8) The risk characterization in Table 6 indicates that, for the inhalation receptor exposures considered:

- The exposures potentially associated with outdoor air quality, for adults, youth and children, fall in the lower 3% range of the air quality guidelines of various jurisdictions.
- Exposures associated with typical outdoor exposure (ie. 3 hr) fall in the lower 1 % range of the air quality guidelines of various jurisdictions
- Exposures associated with personal activity patterns fall in the lower 2% range of the air quality guidelines of various jurisdictions.

It should be noted that these air quality guidelines may be of different types. Some are purely health based and some are regulatory and therefore may have been influenced by various risk management considerations. The regulatory guidelines may also have different uses (eg. judging the acceptability of air quality per se or judging the incremental addition by a source to the existing air quality).

9) Table 6 also indicates that all the inhalation exposures are less than the range of occupational levels.

10) MOEE is presently reviewing the basis of the existing standard for cadmium.

#### Summary and recommendations:

♦ All the inhalation exposures, except exposures associated outdoor air quality (ie. 100 % outdoor exposure) are less than the range of available chronic acceptable exposure levels. Therefore, there is a possibility of long-term health effects associated with outdoor air quality (ie. 100 % outdoor exposure). Because of the possibility of long-term health effects, it is recommended that cadmium should be considered a candidate for reduction of exposure.

♦ The range of estimated inhalation risks associated with 'outdoor air quality' (ie. 100% outdoor exposure) is between  $2.9 \times 10^{-6}$  and  $1.7 \times 10^{-5}$ . Similarly the range of risks associated with 'typical personal exposures' is between  $1.1 \times 10^{-6}$  and  $1.1 \times 10^{-5}$ . Since these levels of risk exceed  $1 \times 10^{-5}$ , a level generally deemed to be negligible, it is recommended that cadmium be considered a candidate for reduction of exposure.

♦ Exposures and therefore risks associated with 'typical personal exposures' and the risks associated with 'outdoor air quality' are similar.

♦ The outdoor, commuting and smoke-affected indoor environments are the most dominant in the upper range of 'typical personal exposures'.

♦ The exposure that a smoker experiences is considerably higher (ie. associated risks are between  $2.3 \times 10^{-4}$  and  $2.8 \times 10^{-3}$ ) than any of the exposures associated with 'personal activity patterns', 'outdoor air quality' and 'typical outdoor exposures'.

♦ Ingestion and dermal exposures exceed inhalation exposures. However, in view of the lack of evidence of the carcinogenicity of cadmium compounds administered orally to experimental animals and the lack of availability of human studies, it is unlikely that these exposures will add to the cancer risk from exposure to ingested cadmium.

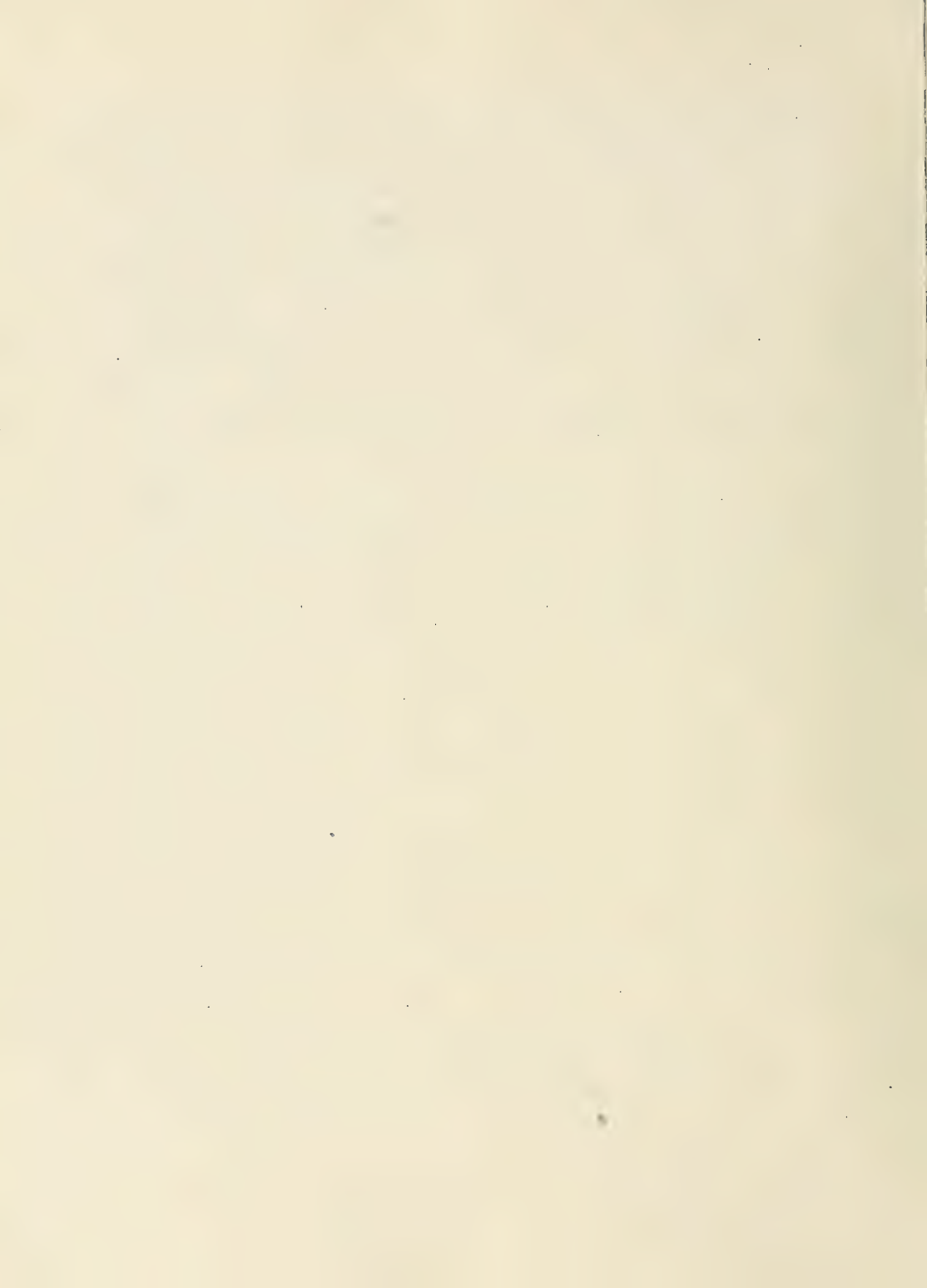
♦ The amount of cadmium that may be ingested from food and from drinking water are less than the corresponding U.S. EPA oral RfDs. These oral RfDs were set to prevent systemic, non-carcinogenic effects.

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APPENDIX 7

RISK ANALYSIS FOR CHROMIUM



APPENDIX 7  
RISK ANALYSIS FOR CHROMIUM

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## CHROMIUM

### DESCRIPTION and SOURCES of CHROMIUM

Chromium is a naturally occurring metallic element found in rocks, animals, plants, and soil. It is present in the environment in several different forms (ie. oxidation states). The most common forms are the metal, which is chromium 0, chromium III, and chromium VI. Chromium III occurs naturally in the environment, whereas chromium VI and chromium 0 are generally produced by industrial processes. Chromium VI, also called hexavalent chromium, is the most important toxicologically.

Chromium compounds, mostly in chromium III or chromium VI forms, produced by the chemical industry are used for chrome plating, the manufacture of dyes and pigments, leather, wood preservative, and treatment of cooling tower water.

Continental dust is the main source of natural chromium present in the environment. Much larger amounts of trivalent and hexavalent chromium are released to the environment from human activities such as: steel, refractory and chemical manufacturing; municipal incineration; and as a constituent of sewage sludge. Industrial cooling towers and chrome plating facilities are sources of hexavalent chromium. Chromium ore refining, cement production, and coal and oil combustion are likely sources of trivalent chromium.

#### 1. HAZARD IDENTIFICATION

##### 1.1 Absorption and Metabolism

Various aspects of absorption are discussed in sections 3.1 and 3.2.

##### 1.2 Toxicology

###### 1.2.1 Evidence for carcinogenicity.

The International Agency for Research in Cancer (IARC) classifies Cr VI as a Group 1 carcinogen (sufficient evidence for causing lung cancer in humans) and US-EPA designates it as a Class A carcinogen, but only by inhalation. These classifications are based on epidemiological studies that have shown an increased risk of lung cancer from occupational exposure to airborne particulates in industries using bichromate ( $\text{Cr}_2\text{O}_7^{2-}$ ) and chromate ( $\text{CrO}_4^{2-}$ ) for the manufacture of pigments and alloys, and for the welding of stainless steel and other alloys containing chromium. Neither inhaled Cr VI nor Cr III have been shown to cause increased incidence of lung tumors in animal studies, although tumors have been produced by implantation and intramuscular and subcutaneous injection of Cr VI in animals. Trivalent chromium compounds have not been reported as carcinogenic by any route of exposure.(1,2)

Cr VI is a consistently positive mutagen in both human and nonhuman *in vitro* studies. There is no evidence that Cr III can act as a mutagen *in vitro* assays since it cannot cross cell membranes. Human *in vivo* assays with Cr VI have produced mixed results, but nonhuman assays have yielded consistently positive results for mutations. (1,2)

###### 1.2.2 Evidence for other toxic effects

Occupational exposures to high airborne concentrations can lead to adverse effects on the upper respiratory tract of humans, such as ulceration of nasal and oral mucosa. Slight decrements in lung function have also been observed. There is no evidence that environmental exposures can produce these

effects on the mucosa.

Chromates are potent skin irritants and can induce allergic contact dermatitis in environmentally exposed workers. Less than 10% of exposed workers developed allergic contact dermatitis. The percent of the general population sensitized to chromium has been decreasing over the years and is currently about 2.2% in North America. No studies have been conducted to identify the threshold dose needed to sensitize healthy humans.(1)

Dermal exposure to large amounts of chromate can also lead to kidney damage, especially if skin lacerations are present to facilitate absorption. (1)

Animal studies have shown that chromium has low toxicity via the oral route. Such studies have also shown that low doses of Cr VI are converted to Cr III in the gastrointestinal tract.(1)

### 1.2.3. Chromium as an essential element

The exact level of Cr intake needed for good health is not known, but based on the lack of observed effects of Cr deficiency, an average intake of 10-200 ug/day (depending on age) is "adequate and safe" (dietary allowances recommended by the USA National Academy of Sciences). Chromium deficiency leads to glucose intolerance in humans and rodents and this intolerance can be reversed by dietary treatment with Cr III. (Ref. 10; p.6-1 *et seq*)

## 2. DOSE-RESPONSE INFORMATION/CURRENT EXPOSURE GUIDELINES

The uncertainties surrounding the potential toxicological effects of environmental chromium on communities have influenced significantly the methodologies used to set guidelines and permissible exposure levels. As previously noted, the adoption of reasonably conservative assumptions is warranted in this context in order to provide sufficient protection of public health. This section summarizes various health criteria values, that is, exposure guidelines and dose-response information that leading regulatory agencies (and other relevant sources) have proposed and consider appropriate for permitting facilities, assessing, and characterizing risks associated with various exposures. Potential exposures to chromium are evaluated in section 3 and the risk characterization is presented in section 4.

### 2.1 Air Guidelines

#### 2.1.1 Chronic, Non-Carcinogenic Health Effects

The California Department of Health Services has developed for chromium, in January 1992, an inhalation chronic AEL (ie. Acceptable Exposure Level) of 0.002 ug/m<sup>3</sup>. These values are used for the evaluation of the potential noncancer adverse health effects of long-term (chronic) exposures (18).

The US-EPA's inhalation Reference Concentration (RfC) for chromium is pending (3). EPA defines an RfC as an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily exposure for the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious non-cancer effects during a lifetime.

Generally, the inhalation chronic AEL and the inhalation RfC, are comparable in their use for assessing chronic effects (except carcinogenic effects) due to inhalation.

### 2.1.2 Ambient Air Quality Guidelines

Various jurisdictions have established annual air quality guideline values for total chromium and Cr VI. For the jurisdictions of North Carolina, Massachusetts, Michigan, New York, and Texas the annual average guidelines range between 0.00008 - 0.68  $\mu\text{g}/\text{m}^3$  for total chromium (21). The range is between 0.0008 and 0.025  $\mu\text{g}/\text{m}^3$  for Cr VI (21).

The ambient air quality criterion and the half-hour point of impingement value in Ontario for all forms (i.e. di-, tri-, and hexavalent forms) of chromium are 1.5 and 5  $\mu\text{g}/\text{m}^3$  respectively.

### 2.1.3 Occupational Guidelines

Occupational exposure limits have been developed for chromium. The American Conference of Industrial Hygienists (ACGIH) presently has a threshold limit value (TLV) of 50  $\mu\text{g}/\text{m}^3$  (22).

The current Ontario occupational limit for chromium is also 50  $\mu\text{g}/\text{m}^3$ . A new value of 20  $\mu\text{g}/\text{m}^3$  was recently proposed (23) based on a recent review of five jurisdictions, with the most stringent value having been selected.

### 2.1.4 Carcinogenic effects

Since there is no evidence for chromium being a carcinogen by any other route except inhalation, US-EPA has only developed a unit risk value (lifetime risk due to hexavalent-chromium in air) of  $1.2 \times 10^{-2}$  per  $\mu\text{g}/\text{m}^3$  for this route (3; 10, p.7-79 *et seq*). The equivalent potency is 41  $(\text{mg}/\text{kg-d})^{-1}$ . This value is based on the occupational epidemiological studies by Mancuso (1975) of chromate production facilities in the United States. A multi-stage, extra risk dose extrapolation method was used. The cancer mortality was assumed to be due to Cr VI, which was further assumed to be no less than one-seventh of the total chromium (ratio of Cr III to Cr VI is 6:1). It was also assumed that the smoking habits of chromate workers were similar to those of the USA white male population.

Epidemiological studies of chromate production facilities in other countries have established an association between chromium exposure and lung cancer. Most of these studies did not attempt to determine whether Cr III or Cr VI compounds were the etiologic factors. Three studies of the chrome pigment industry also found an association between exposure (predominantly to Cr VI) and lung cancer. Two studies of the chromium plating industry were inconclusive and one was negative. Three studies of ferrochromium workers were inconclusive.

The assumption in the Mancuso study that the ratio of Cr III to Cr VI is 6:1 may lead to a 7-fold underestimation of risk. The use of 1949 hygiene data, which may have underestimated worker exposure, may result in an overestimation of risk as may the assumption regarding smoking habits, since it is generally accepted that the proportion of smokers is higher in industrial workers than in the general population. The upper and lower bounds of the unit risk estimate, allowing for all of the uncertainties, are  $8.4 \times 10^{-2}$  and  $3.0 \times 10^{-3}$  (10).

The California Department of Health Services (CDHS) has established an inhalation unit risk of  $1.4 \times 10^{-1}$  associated with lifetime continuous exposure to 1  $\mu\text{g}/\text{m}^3$  (18). This is equivalent to a potency of 500  $(\text{mg}/\text{kg-d})^{-1}$ . The ratio of the CDHS to US-EPA potencies is 12. Part of this difference is explained by CDHS's choice of 500 in the range of potencies 60-3200, but the largest difference is due to EPA's use of the maximum likelihood estimate instead of CDHS's use of the upper 95% confidence bound estimate on potencies derived from human data.

The World Health Organization (WHO) in its air quality guidelines publication (20) noted that at an air concentration of  $1 \text{ ug/m}^3$  of hexavalent chromium, the estimated lifetime risk is estimated to be  $4 \times 10^{-2}$ . This is based on three epidemiological studies and the average risk assessment model. Both the data set and the model used are different from the ones used by EPA.

The above guidelines for atmospheric chromium are summarized in Table 1 below.

## **2.2 Other Route Guidelines**

### **2.2.1 Oral RfD.**

US-EPA has derived a value of  $5 \times 10^{-3} \text{ mg/kg-day}$  or  $5 \text{ ug/kg-day}$ . This RfD is based on a one-year drinking study with rats (MacKenzie *et al*, 1959). No effects, except for a reduction in water consumption, were observed at a dose of  $25 \text{ mg/L}$  of  $\text{K}_2\text{CrO}_4$ , converted to  $2.4 \text{ mg Cr VI/kg-day}$ . This NOEL was divided by an uncertainty factor of 500 to obtain the RfD. The RfD is limited to soluble salts of Cr VI. The confidence in the RfD is rated as *low*.

Although not explicitly stated, any possible contribution of Cr VI from food is not taken into account when setting the RfD.

### **2.2.2 Maximum allowable concentration (MAC) in drinking water in Ontario.**

The MAC has been established at  $50 \text{ ug/L}$ , based on human health considerations (12). The rationale is that at this concentration "hexavalent chromium has not had any known harmful effects on the health of man or animals. Data available are insufficient to determine whether higher concentrations would be equally safe". In chlorinated drinking water, chromium is present as hexavalent as the trivalent is oxidized.

Although not explicitly stated, the amount of Cr VI ingested from drinking is presumably in addition to the amount ingested from food and other sources. Assuming a concentration of  $50 \text{ ug/L}$  in the drinking water and a consumption of  $1.5 \text{ L/day}$ , the maximum additional exposure allowed by the MAC is  $75 \text{ ug/day}$ .

The above ingestion guidelines are summarized in Table 1.

## **3. HUMAN EXPOSURE ASSESSMENT**

The most recent US-EPA proposed guidelines for exposure estimates state that it is inappropriate to conduct a health risk assessment by only considering a worst-case approach unless it is for initial screening purposes (11). This exposure assessment for chromium estimates the most plausible exposures for the general population of Windsor and assigns, wherever possible, upper and lower bounds to the estimate.

### **3.1 Inhalation**

#### **3.1.1 Ambient Air Quality**

Ambient outdoor levels of total chromium have been measured at eleven fixed site stations in Windsor by the Ontario Ministry of Environment and Energy. For this assessment, data from all these sites were available. The measurements include four years of data and 2838 samples, each collected over a 24 hour period. Concentration levels range from non-detectable to  $140 \text{ ng/m}^3$ , with the mean (average), 90th percentile and 95th percentile levels being 6, 20, and  $30 \text{ ng/m}^3$  respectively.



TABLE 1. Summary of Exposure Guidelines for Chromium VI from Leading Agencies

GUIDELINE APPLICATION	AGENCY(IES)	ORIGINAL VALUE	CONCENTRATION ("Original Form" converted to these -as applicable)			CALCULATED "ALLOWABLE" INTAKE (3)
			Unit Risk (1)	R5C (2) (1 x 10 <sup>-6</sup> )	R5C (2) (1 x 10 <sup>-6</sup> )	
INHALATION GUIDELINES						
Occupational	ACGIH, Ontario	20,000-50,000 ng/m <sup>3</sup>	NA	NA	NA	400,000 - 1,000,000 (5700 - 14300)
Ambient Air Quality Guidelines	US states,	0.08-680 ng/m <sup>3</sup> (Tot. Cr.) 0.8-25 ng/m <sup>3</sup> (Cr VI)	NA	NA	NA	1.6 - 13600(Tot. Cr) 16 - 500 (Cr VI)
Ontario Air Quality Guideline (5)		1500 ng/m <sup>3</sup>	NA	NA	NA	30,000 (430)
Chronic AELs/RfCs	CDHS	2 ng/m <sup>3</sup>	NA	NA	NA	40 (0.6)
Inhalation Cancer Potency Factor	EPA EPA(Lower bound) EPA(Upper bound) CDHS WHO	See Unit Risk column	1.2 x 10 <sup>-2</sup> 3.0 x 10 <sup>-3</sup> 8.5 x 10 <sup>-2</sup> 1.4 x 10 <sup>-4</sup> 4.0 x 10 <sup>-2</sup>	0.8 3 0.1 0.007 0.25	0.08 0.3 0.01 0.007 0.025	for 1 x 10 <sup>-6</sup> risk: 1.4 - 60 (0.02 - 0.86) for 1 x 10 <sup>-6</sup> risk: 0.14 - 6 (0.002 - 0.09)
INGESTION GUIDELINES (4)						
Drinking Water Guideline	Ontario	50,000 ng/L	NA	NA	NA	75,000 (1070)
Chronic RfD	EPA	5000 ng/kg-day	NA	NA	NA	350,000

<sup>1</sup>For inhalation guidelines, unit risks are expressed as (ug/m<sup>3</sup>)<sup>-1</sup>.

<sup>2</sup>For inhalation guidelines, risk specific concentrations are expressed as ng/m<sup>3</sup>.

<sup>3</sup>Intake was computed by assuming, where applicable, an adult weight of 70 kg, a breathing rate of 20 m<sup>3</sup>/day, a water intake of 1.5 L/day. In all cases 100% bioavailability of the intake was assumed.

<sup>4</sup>Since there is no evidence for chromium being a carcinogen by any other route except inhalation, no oral cancer potency factors are available (or need to be considered) Ontario guideline applies to all forms (i.e. di-, tri-, and hexavalent) of chromium.



From the inhalation point of view, chromium VI, rather than total chromium, is the form of concern. There is limited information on the fraction of total chromium that is chromium VI.

Falerios *et al* (7) measured ratios of CrVI to total Cr at a chromium contaminated site, for indoor and outdoor environments, as 0.21 and 0.25, respectively. For an 'uncontaminated' site, the ratio of CrVI to total Cr, in indoor environments, is 0.15. They also state that Cr VI makes up about 1-5% of the total Cr in soils.

A study (8) of two ferrochrome smelter dusts indicates that the respirable particles (<10  $\mu\text{m}$ ) are enriched in bioavailable Cr VI and the large chromite-like particles containing primarily insoluble Cr III. The first ore had about 19% present as Cr VI; the second, 4%. The results of these two studies suggest that the amount of Cr VI in suspended particulates is variable, even in dust from the same source; that the ratios indoor and outdoor differ; and that suspended particulates are enriched relative to the soil since the finer size fractions are likely to become suspended or that soil is not the only source of suspended chromium.

Preliminary, chromium VI-specific measurements at a few sites in Windsor (ie. at sites where the extensive total chromium data, noted above, were obtained) indicate that chromium VI ranges between 17 and 24 % of total chromium. It needs to be noted that the total chromium and chromium VI measurements are obtained by different methodologies (see Ref.25. for more detailed discussion). Further investigations in this area are continuing. However, these preliminary findings are in line with the finding of others and therefore, for this assessment, the assumption that the percentage of chromium VI in total chromium is 20 % in ambient and indoor air is not unreasonable.

It is possible to estimate the daily intake of chromium VI associated with these measures of Windsor ambient air quality, recognizing that personal real exposures/intakes may be quite different as further discussed in section 3.1.2. Table 2 below shows these estimated intakes for two different receptors, i.e., an adult and a child. It should be noted that these intakes were calculated based on 24 hour exposures and assume 100% bioavailability by the inhalation route.

**Table 2. Estimated Daily Intakes of Chromium VI Associated With Ambient Air Quality in Windsor**

Air Quality Measure (a)	Concentration (Total Cr) ng/m <sup>3</sup>	Concentration (Cr VI) (c) ng/m <sup>3</sup>	Adult (b) ng/day (ng/kg-day)	Child (b) ng/day (ng/kg-day)
Mean	6.0	1.2	24 (0.34)	6 (0.4)
90th percentile	20.0	4.0	80 (1.14)	20.0 (1.3)
a) Based on 2838, 24 hour average samples b) Assuming the following weights and inhalation rates per day (ie. per 24 hour period): Adult: 70 kg; 20 m <sup>3</sup> /day Child: 15 kg; 5 m <sup>3</sup> /day c) Assuming that Cr VI is 20 % of the total chromium.				

The absorption from the lungs depends on factors such as the physical and chemical properties of the particles (oxidation state, size, solubility), the activity of alveolar macrophages and the reaction of the particles with the respiratory mucosa. The absorption has been studied in both animals and man (9, p.55; 26, p.49).

Particles and droplets greater than about 5  $\mu\text{m}$  do not penetrate into the alveoli of the lungs but are deposited in the nasal passages, trachea and bronchi and are cleared by ciliary action and swallowed. Smaller particles, especially those <2  $\mu\text{m}$  do penetrate to the lungs and are deposited there. The amount deposited is about 30%. The remainder is swallowed.

Deposited Cr VI compounds are, in most cases, absorbed more rapidly than Cr III compounds. Studies with intratracheal injection show that 53-85% of Cr VI compounds (<5  $\mu\text{m}$ ) are cleared from the lungs by absorption and mucociliary clearance in the pharynx, but that only 5-30% of Cr III compounds are absorbed (9, p.56). Other studies have shown that, ten minutes after injection, only 15% of soluble chromate remained in the lung but that 70% of Cr III remained. After 60 days, the corresponding numbers were 1.7% and 13%. The absorption of Cr III compounds also depends on their solubility, with lead chromate being cleared more slowly than sodium chromate (26, p.49).

What the studies suggest is that, for continuous exposures, perhaps 80-90% of the particles that reach the lung are absorbed.

### 3.1.2 Microenvironments

It is reasonable to assume that the daily chromium intakes associated with typical personal exposure patterns can be better estimated from various microenvironmental concentrations than from fixed site monitoring data. For the purpose of scoping population exposures, the set of typical receptors in Table 3 below was considered. Examples of the receptor types and/or their characteristics are also included in Table 3. Using chromium concentrations acquired in various microenvironments, either as part of the personal exposure or subsequent microenvironment study in Windsor, it is possible to scope out various typical personal inhalation exposure scenarios for the above receptors. The estimated daily intakes (in ng/day) of these receptors are summarized in Table 4.

Table 3. Receptors With Typical Personal Exposure Patterns

NAME OF RECEPTOR TYPE	CHARACTERISTICS	NAME OF RECEPTOR TYPE	CHARACTERISTICS
Average Office Worker (Non-smoking)	Eg. - Typical office worker (Based on Windsor volunteers and US EPA TEAM study; not smoking at home)	High Outdoor Receptor	Eg. - Construction workers; - Bicycle couriers - Police - Long distance runners
Average Office Worker (Smoker Environment)	Eg. - Typical office worker (Based on Windsor volunteers and US EPA TEAM study; smoking at home)	High Indoor Receptor	Eg. - 'Shut-ins'- Invalids - Elderly, non-mobile

Average Youth	Eg. Special exposures at shopping malls and athletic facilities (pools) in addition to school;	High Commuting Receptor	Eg.- Bus drivers - Taxi drivers - Delivery/ Distribution Services
Average Child (Non-Smoker Home & No Exposure to Tobacco Smoke)	Eg. Similar to average office worker except 'School' replaces 'Office';	Active Receptor # 1	Eg.- 7 hr/week in Bingo Hall or Bar
Average Child (Non-Smoker Home & Typical Exposure to Tobacco Smoke)	Eg. Includes typical times that children may be in proximity to tobacco smoke, outside the home, based on activity pattern studies;		
Average Child (Smoker Home with Exposure to Tobacco Smoke)	Eg. Child living in a house where there is a smoker		

In order to place these inhalation exposures (ie. intakes) in Windsor in perspective, it is appropriate to compare to daily intakes that people who smoke may experience.

### 3.1.3 Smoking.

Smokers are a significant minority of the population. The chromium content of cigarette tobacco in the United States has been reported to be 0.24 - 6.3 ug/g, but neither the chemical form nor the amount of chromium in tobacco smoke is known with any certainty.(9; p.131). Guerin *et al* (14; table 12.7) state that the Cr content of tobacco ranges from 0.4 - 10 ug/g. Since cigarettes typically contain one gram or less of tobacco and the transfer percentage to mainstream smoke ranges from <0.02% up to 10%, depending on the metal, then the amount of Cr in mainstream smoke is <0.1 ug/cigarette. An upper bound to the exposures from cigarette smoking, assuming a pack per day (25 cigarettes), is 2.5 ug/day (2500 ng/day), or = 40 times the exposure in other environments.

Non-smokers who are heavily exposed to environmental tobacco smoke inhale the equivalent of 1/3 to 3 cigarettes per day or <30 to 300 ng of chromium/day (Blot and Fraumeni<sup>16</sup>). Vainio<sup>26</sup> states that the exposure of non-smokers to environmental tobacco smoke would be about 1% of that of active smokers or 25 ng/day, whereas Remmer<sup>17</sup> gives as an upper limit the equivalent of only 1/5 of a cigarette per day or <20 ng/day. Hiller<sup>27</sup>, quoting other authors, gives intakes ranging from a low of 0.001 cigarette equivalents (CE)/hr or 0.01 CE/day, assuming 12 hr exposure, to a high of 27 CE/day. The higher value is clearly anomalous as the range claimed by the other authors is 0.001 to 0.2 CE/hr. The lower value suggested by Hiller gives an intake of <25 ng/day. About 50-80 % of the inhaled smoke is deposited in the lungs and it is reasonable to assume that the chromium on the smoke aerosol(16, 28) is absorbed to the same extent as particulate chromium.

Furthermore it is also important to place the inhalation exposures (ie. intakes) in Windsor into perspective, relative to general exposures from other media (ie. see section 1.3.2).

Table 4. Estimated Daily Intakes (ng/day) of Chromium VI, Associated with Typical Personal Exposures (See footnote 1\*)

MICRO ENVIRONMENT	Air Concentration (Cr VI) (ng/m <sup>3</sup> ) (h)	Average Office Worker Non-smoker	Average Office Worker Smoker Home Environment	Youth	Average Child Non smoker/ home/No exposure to tobacco smoke	Average Child Non smoker/ home/Typical exposure to tobacco smoke	High Outdoor Receptor	High Indoor Receptor	High Commuting Receptor
Office	0.2/0.5 (m)	6.7(a)	6.7(a)				1.7		
School	0.2/0.5 (d)			6.7	6.7	6.7			
Home	0.4/0.7 (m)	13.3(b)		13.3	13.7	12.4	13.7	20.4	13.7
Communting (in-transit)	1.2/4 (m)	1.0(a)	1.0(a)	1.0(f)	1.0(f)	1.0(f)	1(a)	1(a)	7.7
Urban (Outdoors)	1.2/ 4	2.6(a)	2.6(a)	2.6	2.6	2.6	7.6(g)	2.6	2.6
Home with smokers	0.88/0.94 (c)		13.7(b)			1.3(e)			
Shopping Mall/Market	0.2/0.5 (k)	0.4(i)		0.4(i)					
Bar or Bingo Hall	0.5/0.6								
INTEGRATED EXPOSURE (ng-hrs/m <sup>3</sup> )		11.1/ 27.3	17.7/ 30.6	11.1/ 27.3	11.1/ 27.3	11.8/ 27.7	16.1/ 44.8	12.5/ 28.7	17.8/ 50.8

TIME WEIGHTED AVERAGE EXPOSURE (ng/m <sup>3</sup> over 24 hr) (h)	0.5/1.1	0.7/1.3	0.5/1.1	0.5/1.1	0.5/1.1	0.5/1.2	0.7/1.9	0.5/1.2	0.7/2.1
INTAKE/DAY (NG/DAY) (h)	9.2/22.7	14.8/25.5	6.5/ 15.9	2.3/5.7	2.5/5.8	13.5/37.4	10.4/23.9	14.9/42.3	



### Estimations:

\* INTEGRATED EXPOSURE (ng-hrs/m<sup>3</sup>) = SUM OF [Microenvironment concentration x Time spent in Microenvironment]

\* TIME WEIGHTED AVERAGE EXPOSURE (ng/m<sup>3</sup>) = INTEGRATED EXPOSURE/24 hr

\* INTAKE/DAY (ng/day) = TIME WEIGHTED AVERAGE EXPOSURE x DAILY BREATHING RATE (ie. for Adult or Youth or Child as applicable)

### Footnotes:

- a.) TIME BUDGET ANALYSIS; Windsor '91 Summer PEP Study; Handout to Volunteers; May/92 (R. Bell)
- b.) Sum of 'Indoor, Home' and 'Indoor Other' in a.)
- c.) Determination of the contribution of tobacco smoke to indoor levels of chromium VI is still in the development stage. These values were obtained during the personal exposure study in Windsor from homes where smoking was permitted.
- d.) Assumed to be same 'microenvironment' concentration that were measured by PEP study in the 'Office' environment.
- e.) Average time spent in proximity to tobacco smoke, in various locations outside the home, was approximately 1.3 hours, based on a study of children's activity patterns; (Ref: Study of Children's Activity Patterns, State of California, Air Resources Board, Contract No. A 733-149). Assume that chromium concentrations, when in proximity to tobacco smoke is represented by the levels referenced in footnote "c," above.
- f.) Assume 1 hour is spent in the car per day.
- g.) For the 'high-outdoor' receptor, urban outdoor concentrations were assumed to be represented by the 'mean' and 90th percentile concentrations taken from the fixed site monitoring network. Also assume that for this group, the 6.7 hours of 'at work' exposure is divided so that 1.7 hours is spent in the office and 5 hours is added to the 2.6 hours of urban outdoor exposure for a total of 7.6 hours.
- h.) First number is the 'mean'. The second number is the 90th percentile, if available (otherwise it is the maximum value measured), of Cr VI. It was assumed that Cr VI is 20 % of total chromium.
- i.) Assumed that approximately 2.8 hours per week are spent on malls shopping; this was distributed over seven days yielding '0.4 hours/day' on malls.
- j.) Assumed that this receptor spends approximately 7 hours per week in a bingo hall or bar; this was distributed over seven days yielding '1 hr/day' in bingo halls or bars.
- k.) No values were available for these microenvironments. Levels assumed to be the same as found in the 'office'.
- l.) Two additional typical personal exposure patterns that were evaluated but are not shown in detail in this table are the 'Average Child in a Smoker Home' and the 'Active Receptor #1' as noted in Table 3 above. The corresponding intakes/day (ie. mean/90th percentile) for these two receptors are 3.7/6.4 and 9.4/22.7, respectively.
- m.) The 'mean' and '90th percentile' concentrations for the 'Office', 'Home' and 'Commuting' microenvironments were derived from the Summer 1991 and Winter 1992 personal exposure studies in Windsor.

### 3.2 Other Routes

In this section, possible non-inhalation routes of exposure (ie. ingestion and dermal) are assessed.

#### 3.2.1 Ingestion of Food

The bioavailability of chromium in various matrices determines the amount that is absorbed into the blood stream from the gastrointestinal tract. Bioavailability is a measure of the degree to which the ingested (or inhaled) dose of a substance becomes physiologically available to the body tissues, depending upon absorption, distribution, metabolism and excretion rates.

If the guideline, such as an RfD, to which the amount of ingested chromium is compared, is derived from ingestion studies, then the differences in the bioavailability are likely to be small even if the studies are based on rodents, and, need not be considered. For other routes of exposure, the differences in bioavailability have to be allowed for.

Experiments with dissolved chromium in humans and rodents show that absorption from the gastrointestinal tract is not quite constant. (Ref. 9, p.56-57; Ref. 10, p.5-4 *et seq*). The experiments indicate that:

- the amount absorbed is quite small (0.5-2.0%), since Cr VI compounds are reduced to Cr III in the stomach and both valence states are bound by acid gastric juices;
- the amount depends on:
  - the dietary intake in humans (at 10ug,  $\approx$  2% is absorbed; at  $\geq$ 40 ug, the absorption efficiency drops to  $\approx$  0.5%);
  - the valence state of the Cr, with the absorption efficiency of Cr VI being 4 to 25 times that of Cr III;
  - the matrix for the Cr; some chelating agents, which are naturally present in foods, may enhance absorption;
  - fasting increases the absorption.

The amount of information on the average daily intake of chromium is meagre. The following values (taken from ref.2; last one from ref.12)- presumably for adults - have been reported (in ug/d of Cr):

United States	60-280	(1977)
Japan	130-254	(1965)
United Kingdom	320 $\pm$ 162	(1979)
Italy	50	(1976)
India	150	(1969)
Canada	136-152	(1974)
	55 (10 -160)	(1984)

HCB has calculated a value of 250 ug Cr/day for a child and 280 for adults from concentrations measured by Health and Welfare in the Ottawa-Hull area in 1976, using the 1976 HWC food consumption data (2).

The International Commission on Radiological Protection estimates an average intake of 150 ug

Cr/day for an average diet (2).

These intake figures are for total chromium. There appears to be no information on the amount in food that is bioavailable. The assumption can be made that it is the same as in drinking water. Chromium occurs mainly in trivalent form in food, although in some foods up to 2/3 is present as hexavalent (12).

### 3.2.2 Drinking Water

The MOE monitors both the raw and treated water at the Windsor water treatment plant 6 to 8 times per year. The mean concentration (14 samples) in the treated water in 1990 was 2.4 ug/L and in 1991, 2.0 ug/L (detection limit - 0.1 ug/L). The median concentration for these two years was 2.1 ug/L and the 90th percentile about 3.5. The range was 0.7 to 4.5 ug/L. A survey of trace metals in the Great Lakes indicates that the median concentration in Lake Huron is 0.13 - 0.3 ug/L (13).

A survey of tap water consumption in Canada was done in 1977/78 by Health and Welfare Canada (4). The intake covers both tap water drunk directly and tap water based fluids such as coffee, tea, soup etc. The overall Canadian average for the 18 and over age group is 1.49 L/d, with 90% of the group consuming <2.59 L/d. The mean for children <6 yr is 0.76 L/d, with 90% of this population consuming <1.5 L/d.

In the area served by the Windsor water treatment plant, the intakes of chromium from tap water and tap water based fluids, using 2.1 ug/L as the median concentration, is:

adults:	mean:	3.2 ug/d
	90th percentile*:	5.4 ug/d.
children:	mean:	1.6 ug/d
	90th percentile*:	3.2 ug/d

\* Based on the amount of water consumed.

About 10% of the chromium in surface waters of the upper Great Lakes is in the particulate phase (13). The dissolved chromium in drinking water is converted to the hexavalent form by chlorination (12).

There is no information on the bioavailability of the particulate chromium but it is assumed to be the same as for the dissolved Cr for the purpose of this assessment.

### 3.2.3 Soil

Total chromium was measured in soils in the Windsor area in 1990. The surface samples were collected in lawns and parks. The mean concentration for the stations in Windsor itself is 24.5 ug/g (standard deviation - 3.7). The median concentration is 23 ug/g and the 90th percentile is approximately 28 ug/g. The range in concentrations is 18 - 36. The concentrations in the rural area around Windsor are not significantly different from downtown Windsor (median - 23 and 90th percentile - 27).

A reasonable estimate for the amount of ingested soil and dust is 80 mg/day for children and 20 mg/day for adults (2; Appendix 1), although values as low as 0 for children < 1 yr, 40 mg/d for children 1-6 yr and 10 mg/d for persons >6 yr have been used (1). Calabrese and Stanek (15) have

modelled the relative contributions of soil and indoor dust to the total intake of children. They estimate that about 65% is from outdoor soil or in the range of 10 - 36 mg/d, depending on the trace element used for deriving the ingestion amount. The total intake of dust and soil is in the range of 16 - 55 mg/d.

Both Sheehan *et al* (1) and Liroy *et al* (5) differentiate between exposures to household dust and outdoor soil in their risk assessment of exposure to soils contaminated with chromium wastes. This seems an unnecessary refinement for this analysis because of the small amount of ingested Cr and lack of information on the concentration of Cr in household dust. The concentration of chromium in indoor dust is, according to these reports, less than the outdoor soil concentration. Therefore, the estimated intakes calculated below may well overstate the actual amounts.

The median amount of total chromium ingested from soil by adults, using the median concentration and the ingestion amounts from above, is 0.5 ug/day, with 90% of the population consuming <0.6 ug/day. The median amount ingested from soil by children is 1.8 ug/day, with 90% of the children consuming <2.2 ug/day.

There is no information on the bioavailability of the chromium in the Windsor area soils nor on the fraction present as Cr VI. Sheehan *et al* (1) conclude that oral bioavailability is certainly <1-2%. Out of caution, they assume a 10% bioavailability. However, it is unlikely that the bioavailability of chromium in soils exceeds the bioavailability in foods or 0.5 - 2 % (s. 3.2.1). The same study reports that Cr VI makes up, on the average, 5.9% of the total chromium in the soils at the study site.

Falerios *et al* (7) state that Cr VI makes up about 1 - 5% of the total Cr in soil. Chromium is present mainly as the insoluble oxide  $\text{Cr}_2\text{O}_3 \cdot n\text{H}_2\text{O}$  and is therefore not very mobile, although in anaerobic wet soils, soluble complexes may be formed (9; p.123).

### 3.2.4 Dermal

#### 3.2.4.1 During Showering and Bathing

US-EPA (6) has developed models for the dermal absorption of both inorganics and organics. The former assumes a steady-state; the latter allows for a transient state.

The equation for inorganics is

$$\text{DA}_{\text{event}} = K_p C_w t_{\text{event}}$$

where:  $\text{DA}_{\text{event}}$  is the dose absorbed per unit area per event

(mg/cm<sup>2</sup>\*event)

$K_p$  is the permeability constant from water (cm/hr)

$C_w$  is the concentration of a chemical in water (mg/cm<sup>3</sup>)

$t_{\text{event}}$  is the duration of the event (hr/event)

$K_p$  for chromium is  $2 \times 10^{-3}$  cm/hr (Ref. 6; Table 5-3). The median surface area of a child is 0.731 m<sup>2</sup> (6; table 8-4 for age 4<5 years) and the 90th percentile is 0.821. For an adult, the values are,



respectively, 1.94 and 2.28 m<sup>2</sup> (6;table 8-3). These areas are estimated from models and not measured directly.

The median concentration in water at Windsor is 2.1 ug/L or 2.1x10<sup>-6</sup> mg/cm<sup>3</sup>. The chromium is present as Cr VI (see s. 3.2.2). A shower is assumed to take 0.25 hr; a bath, 0.5. The whole body is assumed to be wet for the duration of the once-daily event.

The amounts absorbed during a shower are then

adult:	median body area:	0.02 ug/d
	90th percentile:	0.024 ug/d
child:	median body area:	0.008 ug/d
	90th percentile:	0.009 ug/d

The amounts absorbed during a bath are twice the above values.

#### 3.2.4.2 Contact With Soil and Dirt

Cr III in solution binds readily to skin and is not dermally absorbed to a significant extent. Cr VI is reduced to Cr III by various skin constituents. The dermal absorption of total Cr is likely to be no greater than for oral absorption, or 0.5 - 2%. The most appropriated daily loading of soil on exposed skin is estimated to be 1.8 mg/cm<sup>2</sup> (range 0.5 - 2.8). The exposed area is taken to be 1580 cm<sup>2</sup> for a child and 1980 for an adult, or basically the hands and arms. (1) It is unlikely that the skin is as contaminated in winter as in summer or that the hands and arms are covered by dust 24 hours a day. Therefore, the actual amounts absorbed are likely to be less than the amounts shown below.

Taking all of these factors into account and using the median soil concentration of 23 ug/g (s.3.2.3), the amount absorbed through the skin is:

adults:	0.5 % absorption:	0.4 ug/day
	2 % absorption:	1.6 ug/day
children:	0.5 % absorption:	0.3 ug/day
	2 % absorption:	1.3 ug/day

### 4. RISK CHARACTERIZATION AND PERSPECTIVES

#### 4.1 Inhalation

Exposures, expressed as daily intakes in units of ng/day, were assessed in section 3. Inhalation, ingestion and dermal routes of exposure were considered. Table 5 below summarizes the daily intakes (or ranges of daily intakes) of chromium, for adults and children, estimated in section 3. It should be noted that in section 3, the intakes for inhalation and sometimes for ingestion assumed 100% bioavailability. The intake for dermal exposures are amounts absorbed systemically and hence already include bioavailability considerations. Table 5 has two columns for both adults and children. The first set of columns (ie. '100 % Bioav') give the intakes with 100 % bioavailability having been assumed; the second set (ie. 'Bioav. Incl.'), gives intakes for which



bioavailability has been taken into consideration (ie. if information was available as noted in the footnotes). This second set of columns should give a better picture of the relative importance of various exposure routes. As far as comparison to exposure guidelines and intakes associated with cancer risk, the intakes in the first set of columns of Table 5 will be used (ie. *after appropriate conversion to hexavalent chromium - as in Table 5A for inhalation routes and sections 4.2 to 4.4 for other routes of exposure*), since the exposure guidelines are also expressed as intakes for which we have assumed 100 % bioavailability.

To characterize risks, the various exposure guidelines discussed in Section 2 are compared to the estimated exposures from inhalation and other routes as discussed in Section 3. Because of the assumptions, uncertainties and ranges of values available from both exposures (see Table 5) and the various exposure guidelines (see Table 1), risk characterization is most appropriately done by comparison of ranges of values.

Table 6 below provides a graphic representation of this comparison of exposures, exposure guidelines and intakes associated with inhalation cancer risk, based on ng of hexavalent chromium intake/day (ie. 'INTAKE in Nanograms per day' increasing upwards on the vertical scale).

The middle section of Table 6, "Exposures", depicts the exposures calculated in Section 3, expressed as intake/day (ie. ng/day). The exposures depicted are: *Outdoor Air Quality* - the exposure from spending 100 % of the day outdoors; *Typical Outdoor Exposure* - the exposure from three hours only outdoors, provided for perspective on the contribution to risk solely from contaminants present in outdoor air; *Typical Personal Exposures* - the range of exposures associated with ten different exposure scenarios, combining periods of indoor, outdoor and various microenvironment exposures. Exposure scenarios are included for adults and children, assuming 20 and 5 m<sup>3</sup>/day inhalation rates respectively. For 'outdoor air quality' (ie. 100% outdoor exposure), for 'typical outdoor exposures' (ie. 3 hr), and for the 'typical activity patterns' the ranges shown, bracket the lowest mean to the highest 90th percentile. For perspective purposes, the exposures of smokers, directly from smoking activity is also depicted in this section.

The left section of Table 6, "Exposure Guidelines", expresses the various guidelines discussed in Section 2 in terms of calculated "allowable" intake/day for adults and children. The values are taken from Table 1. Within each type of guideline group (eg. outdoor air) ranges of exposure guidelines, when available, are indicated. Thus, ranges of Air Quality Guidelines (ie. 'Outdoor Air'), Occupational guidelines (ie. 'Workplace Air'), and a chronic health effects based reference concentration (ie. 'Chronic AEL'; only one available) are shown. The MOEE guideline, which includes all forms (ie. di-, tri-, and hexavalent) chromium is shown with a small horizontal bar. Comparison of "Exposure Guidelines" to "Exposures" should be done with care. For example, occupational guidelines are included for perspective purposes only. For caveats regarding this comparison see section 4.1.1 of the main report.

The right section of Table 6, "Intakes Associated With Cancer Risk", shows the intakes associated with different levels of cancer risk. Ranges of carcinogenic risk levels (associated with  $1 \times 10^{-5}$  risk and  $1 \times 10^{-6}$  risk) are depicted. Comparison of "Exposures" to "Intakes Associated With Cancer Risk" is appropriate for adult exposures only, since cancer risk estimates apply to a lifetime of exposure and people are adults for the majority of their lives. Adult exposures in the bars of the "Exposure" section fall in the top 70 % of the bars which represent exposures of adults and children.

Based on the tabular analysis (Table 5 and 5A) and the graphic risk characterization (Table 6), the following observations and deductions can be made:

### Health messages:

1) It is apparent, that the ingestion route exceeds all other exposure routes for chromium. Dermal exposure appears to be next in importance. Inhalation exposure appears to be lowest (ie. for a non-smoker).

2) All the inhalation exposures associated with typical outdoor exposures (ie. 3 hr) are less than the chronic acceptable exposure level - 'Chronic AEL (CA)'- (ie. 40 ng/day from Table 1;) proposed by California (CDHS). However, some of the exposures associated with outdoor air quality (ie. 100% outdoor exposure) and with personal activity patterns exceed this chronic acceptable exposure level by 1.1 to 2.2 - fold. This chronic acceptable exposure level is considered to be purely health based and is protective against all chronic health effects other than cancer risk. Therefore, there is a possibility of long-term health effects associated with the inhalation exposures exceeding the chronic acceptable exposure level.

This comparison of exposures to chronic acceptable exposure levels can also be expressed more quantitatively in the form of a hazard index. These hazard index comparisons for all substances are summarized and are found in section 4.1.5 of the main report.

3) The most conservative range of available exposure guidelines are depicted in Table 6 under Intakes Associated with Cancer Risk. These guidelines were proposed by CDHS, the US EPA, and the World Health Organization. As shown in Table 6, they overlap with and are exceeded by the estimated exposures. Because people are adults for the majority of their lives, these intakes associated with cancer risk are depicted for adults only.

The US-EPA has estimated that a lifetime of exposure to  $1 \text{ ug/m}^3$  of hexavalent chromium will lead to a cancer risk of  $1.2 \times 10^{-2}$  (3,10). The equivalent potency is  $41 \text{ (mg/kg-day)}^{-1}$ . The lower limit of the unit risk estimate is  $3.0 \times 10^{-3}$  [equivalent potency is  $10.7 \text{ (mg/kg-day)}^{-1}$ ] and the upper limit is  $8.48 \times 10^{-2}$  [equivalent potency is  $303 \text{ (mg/kg-day)}^{-1}$ ] to allow for all the assumptions and uncertainties in the data used for the risk derivation (10). Furthermore, CDHS and the WHO have estimated that a lifetime exposure to  $1 \text{ ug/m}^3$  of hexavalent chromium will lead to a cancer risk of  $1.4 \times 10^{-1}$  and  $4.0 \times 10^{-2}$  respectively. The equivalent potencies are 500 and  $143 \text{ (mg/kg-day)}^{-1}$  respectively. These potencies are summarized in Table 7.

The inhalation intakes of Cr VI for adults associated with 'outdoor air quality' (ie. 100 % outdoor exposure), 'typical outdoor exposure' (ie. 3 hr) and 'typical personal exposures' range between 24 - 80 ng/day, 3 - 10 ng/day and 9.2 - 42.3 ug/day, respectively (from Tables 2, 4 and 5 A). These intakes and the corresponding doses in mg/kg-day are summarized in Table 7. Using the various potencies from the three agencies, the range of risks associated with 'outdoor air quality' (ie. 100% outdoor exposure) is between  $3.6 \times 10^{-6}$  and  $5.5 \times 10^{-4}$ . Similarly the range of risks associated with 'typical outdoor exposures' (ie. 3 hr) is between  $4.6 \times 10^{-7}$  and  $7.0 \times 10^{-5}$ . Similarly the range of risks associated with 'typical personal exposures' is between  $1.4 \times 10^{-6}$  and  $3.0 \times 10^{-4}$ . The risks associated with 'typical personal exposures' and the risks associated with 'outdoor air quality' are similar and are slightly higher than the risks associated with 'typical outdoor exposures'. This range of risk analysis is summarized in Table 7. It should be further noted, that this risk characterization (ie. using carcinogenic risk based limits) is based on an assumed lifetime exposure (ie. 24 hours, every day, for 70 years) and hence is a very conservative assumption.

There are several additional uncertainties in estimating the risk in Windsor, most of which will result in a less stringent estimate of risk:

**Table 5. Summary of Estimated Daily Intakes and/or Range of Intakes (in ng /day) of Total Chromium, from Various Exposure Pathways (ie. intakes, assuming 100 % bioavailability and intakes with bioavailability taken into consideration)**

EXPOSURE PATHWAY		ADULT ng/day  (100 % Bioav.)	ADULT ng/day  (Bioav. Incl.)	CHILD ng/day  (100 % Bioav.)	CHILD ng/day  (Bioav. Incl.)
INHALATION	Outdoor Air Quality - Windsor (ie. 100 % outdoor exposure) (a),(g)	120 - 400	32 - 110 (f)	30 - 100	8 - 27 (f)
	Typical outdoor exposure (ie. = 3hr)(b)	15 - 50	4 - 13.8 (f)	3.8 - 12.5	1 - 3.4 (f)
	Typical personal exposures(ie. Table 4) (c), (g)	46 - 211.5	12 - 57 (f)	11.5 - 32	3 - 9 (f)
	Smoking (e)	2500	1500 (f)		
INGESTION	Food (d)	50,000 - 280,000	250 - 5600	50,000 - 250,000	250 - 5000
	Drinking water (d)	3200 - 5400	16 - 110	1600 - 3200	8 - 64
	Soil (d)	500 - 600	2.5 - 12	1800 - 2200	9 - 44
	TOTAL (Ingestion)	53,700 - 286,000	269 - 5720	53,400 - 255,400	267 - 5100
DERMAL (h)	During showering		20 - 25		8 - 9
	Contact with soil & dirt		400 - 1600		300 - 1300
	TOTAL (Dermal)		420 - 1625		308 - 1309
<p>a.) Range of intakes is associated with the range of the 'mean' to '90th percentile' concentrations in outdoor air. It is to be noted that people are not exposed 24 hours to outdoor air. This estimation assumes 100 % exposure to outdoor air and is a measure of outdoor air quality per se and not of actual exposure.</p> <p>b.) Range of intakes calculated from the 'mean' to '90th percentile' concentrations in outdoor air and assuming a 'typical' outdoor air exposure of = 3 hr(ie. corresponding to breathing 2.5 m<sup>3</sup>/3hr for adults and 0.63 m<sup>3</sup>/3hr for children.</p> <p>c.) Range of intakes is estimated from the range of the lowest 'mean' and the highest '90th percentile' concentrations obtained from personal exposure and microenvironment measurements.</p> <p>d.) Gastrointestinal absorption ranges from 0.5 - 2 %. Values in the 'Bioav. Incl' columns were calculated by multiplying the ranges in the '100 % Bioav.' columns(ie. lowest value of the range multiplied by 0.5%; highest value of the range multiplied by 2 %).</p> <p>e.) The intake shown is the direct intake (ie. upper bound estimate) of an adult smoker from smoking activity (ie. 'smoking') only. Various smoking environments for adults and children have already been included in the 'typical personal exposure' scenarios.</p> <p>f.) It is assumed that 30% of the inhaled particles reach the lungs and 90 % are absorbed. (see s. 3.1.1). For smokers, it is assumed that 65 % reaches the lungs (s. 3.1.3).</p> <p>g.) The chromium intakes from Table 2 and 4, were backcalculated to these total chromium values, using the 20 % assumption, in order to allow comparison to intakes from other routes which are for total chromium.</p> <p>h.) Cr III is not significantly absorbed. Therefore, the amount absorbed is mostly as Cr VI. Dermal absorption already takes bioavailability into consideration.</p>					

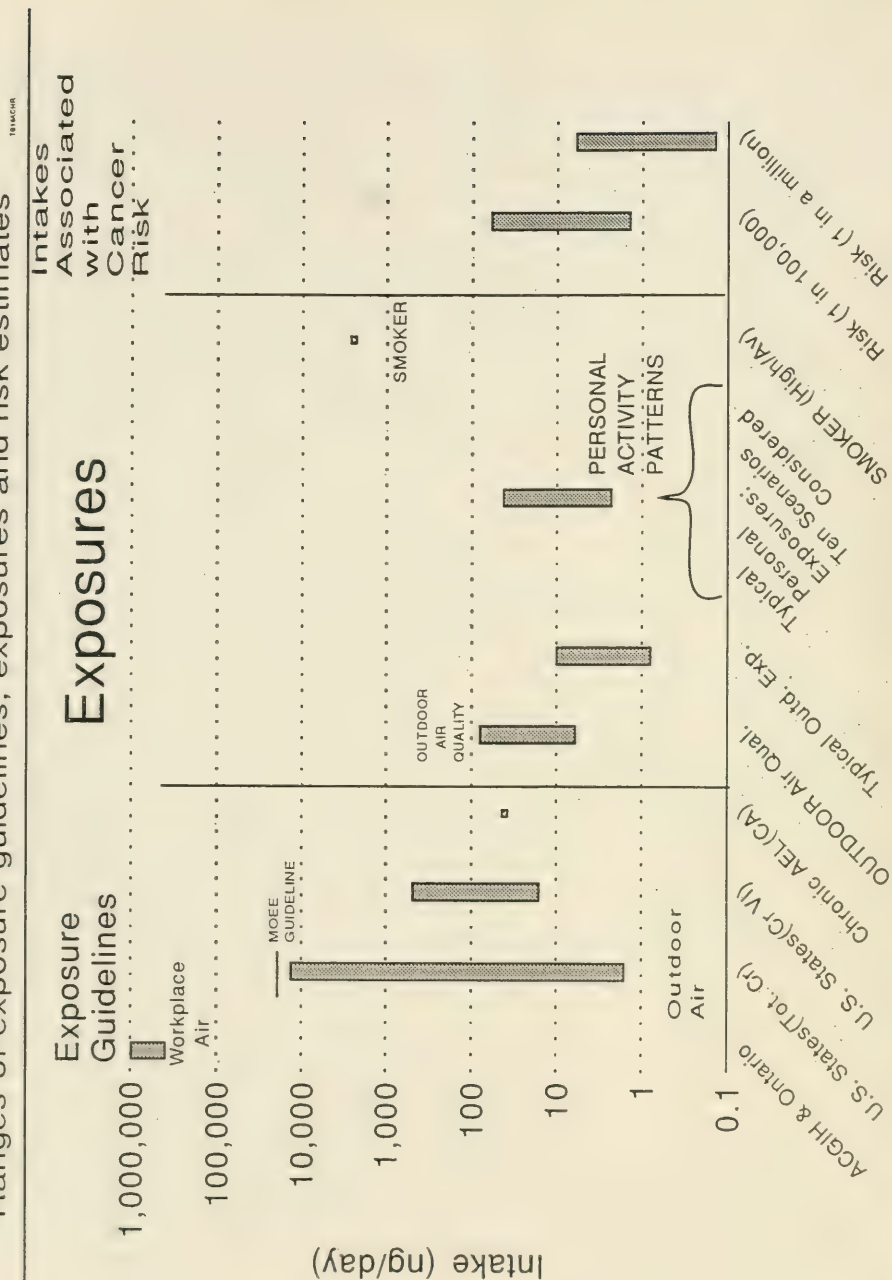


**Table 5 A. Summary of Estimated Daily INHALATION Intakes and/or Range of Intakes (in ng /day) of Chromium VI, from Various Exposure Pathways (ie. intakes, assuming 100 % bioavailability)**

EXPOSURE PATHWAY		ADULT ng/day  (100 % Bioav.)	CHILD ng/day  (100 % Bioav.)
INHALATION	Outdoor Air Quality - Windsor (ie. 100 % outdoor exposure) (a),(d)	24 - 80	6 - 20
	Typical outdoor exposure (ie. $\approx$ 3hr)(b)	3 - 10	0.8 - 2.5
	Typical personal exposures(ie. Table 4) (c), (d)	9.2 - 42.3	2.3 - 6.4
	Smoking (e)	2500 (f)	
<p>a.) Range of intakes is associated with the range of the 'mean' to '90th percentile' concentrations in outdoor air. It is to be noted that people are not exposed 24 hours to outdoor air. This estimation assumes 100 % exposure to outdoor air and is a measure of outdoor air quality per se and not of actual exposure.</p> <p>b.) Range of intakes calculated from the 'mean' to '90th percentile' concentrations in outdoor air and assuming a 'typical' outdoor air exposure of <math>\approx</math> 3 hr(ie. corresponding to breathing 2.5 m<sup>3</sup>/3hr for adults and 0.63 m<sup>3</sup>/3hr for children. c.) Range of intakes is estimated from the range of the lowest 'mean' and the highest '90th percentile' concentrations obtained from personal exposure and microenvironment measurements.</p> <p>d.) Chromium VI intakes from Table 2 and 4</p> <p>e.) The intake shown is the direct intake (ie. upper bound estimate) of an adult smoker from smoking activity (ie. 'smoking') only. Various smoking environments for adults and children have already been included in the 'typical personal exposure' scenarios.</p> <p>f.) Fraction of Cr VI not known; hence assumed to be all Cr VI.</p>			

- The US-EPA unit risk estimate applies strictly to particulate chromium with the same physical and chemical properties as in the Mancuso study used to derive the risk estimate. There is no information available on the physical properties of the particulates in Windsor air, the fraction of Cr VI and the chemical properties of its compounds and on the bioavailability. Information on the fraction of Cr VI in particulates suggests a range from a low of <5% to perhaps 25% (7; the higher figure applies to dust contaminated with chromite ore). A reasonable number of 20% was used in estimating the exposures in tables 2 and 4.
- The unit risk assumes a 70-year residence at a site. Sheehan *et al* (1) state that 30 years is the 90th percentile of the estimated length of residency at one location and 10 years is the 50th percentile in the USA. In setting the unit risk, a 70-year exposure is assumed.
- The risk estimates might be further changed once the bioavailability of the particulate Cr in Windsor air is taken into account. Although Sheehan *et al* (1) assume, for the purpose of their assessment, 100% for all forms of chromium, this is unlikely to be true as it is known that Cr III is absorbed much more slowly from the lungs than Cr VI, possibly as a result of binding to extracellular macromolecules and that water soluble salts undergo conversion to very insoluble moieties with long residence time in lung tissues. The total absorption is  $\approx$ 5% (10;p. 5-1 *et seq*). Since, however, the risk factor was calculated from

Table 6. CHROMIUM VI RISK CHARACTERIZATION in WINDSOR (INHALATION)  
 Ranges of exposure guidelines, exposures and risk estimates





human exposures, the change should not be large, unless the bioavailability of the chromium in the Mancuso study is markedly different from the Windsor particulates.

**Table 7. Range of Inhalation Cancer Risks Associated with Estimated Intakes(ie. for adult exposures only) of Chromium VI.**

RANGE of INHALATION INTAKES			POTENCY (a)		RANGE of RISKS
Environment	Unit ng/day	Unit mg/kg/day	Agency	Unit (mg/kg-d) <sup>1</sup>	
OUTDOOR AIR QUALITY (Windsor)	24 - 80	$3.4 \times 10^{-7}$ - $1.1 \times 10^{-6}$	EPA	41	$1.4 \times 10^{-5}$ - $4.5 \times 10^{-5}$
			EPA (Lower Limit)	10.7	$3.6 \times 10^{-6}$ - $1.2 \times 10^{-5}$
			EPA (Upper Limit)	303	$1.0 \times 10^{-4}$ - $3.3 \times 10^{-4}$
			CDHS	500	$1.7 \times 10^{-4}$ - $5.5 \times 10^{-4}$
			WHO	143	$4.9 \times 10^{-5}$ - $1.6 \times 10^{-4}$
			OVERALL RANGE OF RISKS: $3.6 \times 10^{-6}$ - $5.5 \times 10^{-4}$		
TYPICAL OUTDOOR EXPOSURE (ie.~ 3 hr.)	3 - 10	$4.3 \times 10^{-8}$ - $1.4 \times 10^{-7}$	EPA	41	$1.8 \times 10^{-6}$ - $5.7 \times 10^{-6}$
			EPA (Lower Limit)	10.7	$4.6 \times 10^{-7}$ - $1.5 \times 10^{-6}$
			EPA (Uper Limit)	303	$1.3 \times 10^{-5}$ - $4.2 \times 10^{-5}$
			CDHS	500	$2.2 \times 10^{-5}$ - $7.0 \times 10^{-5}$
			WHO	143	$6.1 \times 10^{-6}$ - $2.0 \times 10^{-5}$
			OVERALL RANGE OF RISKS: $4.6 \times 10^{-7}$ - $7.0 \times 10^{-5}$		
TYPICAL PERSONAL EXPOSURES	9 - 42	$1.3 \times 10^{-7}$ - $6.0 \times 10^{-7}$	EPA	41	$5.3 \times 10^{-6}$ - $2.5 \times 10^{-5}$
			EPA (Lower Limit)	10.7	$1.4 \times 10^{-6}$ - $6.4 \times 10^{-6}$
			EPA (Upper Limit)	303	$3.9 \times 10^{-5}$ - $1.8 \times 10^{-4}$
			CDHS	500	$6.5 \times 10^{-5}$ - $3.0 \times 10^{-4}$
			WHO	143	$1.9 \times 10^{-5}$ - $8.9 \times 10^{-5}$
			OVERALL RANGE OF RISKS: $1.4 \times 10^{-6}$ - $3.0 \times 10^{-4}$		
a. These are equivalent potency factors calculated from the unit risks proposed by the agencies listed; assumed adult weight of 70 kg and 20 m <sup>3</sup> per day.					

4) Although ingestion and dermal exposures dominate over inhalation exposures for chromium, as shown in Table 5, exposure via these non-inhalation routes are not associated with carcinogenic effects and are below the ingestion exposure guidelines (ie. in Table 1) based on chronic endpoints most appropriate for this comparison (see s. 4.2 to 4.4 below).

5) The exposure that a smoker experiences is considerably higher than exposures associated with 'personal activity patterns', 'outdoor air quality' and 'typical outdoor exposures'.

#### Regulatory compliance messages:

6) The risk characterization in Table 6 (ie. using the Cr VI values from Table 5 A) indicates that, for the inhalation receptor exposures considered:

- The exposures potentially associated with outdoor air quality, for adults, youth and children, fall in the lower 20% range of the Cr VI air quality guidelines of various jurisdictions.
- Exposures associated with typical outdoor exposure (ie.3 hr) fall in the lower 2 % range of the air quality guidelines of various jurisdictions
- Exposures associated with personal activity patterns fall in the lower 10% range of the air quality guidelines of various jurisdictions.

It should be noted that these air quality guidelines may be of different types. Some are purely health based and some are regulatory and therefore may have been influenced by various risk management considerations. The regulatory guidelines may also have different uses (eg. judging the acceptability of air quality per se or judging the incremental addition by a source to the existing air quality).

7) Table 6 also indicates that all the inhalation exposures are less than the range of occupational levels.

8) MOEE is presently reviewing the basis of the existing standard for chromium.

#### 4.2 Ingestion.

The following observations and deductions can be made regarding ingestion:

The amount (ug/d) of total ingested chromium, excluding the amount in food, is:

	<u>Child</u>	<u>Adult</u>
Drinking water (Likely all Cr VI)	1.6 - 3.2	3.2 - 5.4
Soil and dust -	1.8 - 2.2	0.5 - 0.6
 Total - ug/d	 3.4 - 5.4	 3.7 - 6.0
- ug/kg*d	0.2 - 0.3	0.05 - 0.09

The body weights are: 16 kg for a child; 70 kg for an adult.

The US-EPA oral RfD (s. 2.2.1) is 5 ug/kg-d based on experiments with rats drinking aqueous solutions of Cr VI. Since the same exposure route applies to both the RfD and the above intakes, the fraction absorbed of bioavailable chromium is likely to be the same and no allowance has to be made for differences in absorption. The ionic form of total chromium in water and soil and dust is not known exactly, but only a few percent in soil and dust is likely to be Cr VI. Assuming that the only ionic form in drinking water is Cr VI, the maximum intake is 6% of the RfD for a child and 1.8% for an adult.

The intakes can also be compared to intakes based on the Ontario drinking water maximum allowable concentration of 50 ug/L of Cr VI. Assuming that an adult drinks 1.5 L/d, the allowable intake is 75 ug/d or 1.07 ug/kg-d. The maximum intakes for a child is then 28% and for an adult, 8% of the allowable intake from drinking water.

Based on the RfD, the total allowable intake of Cr VI for a 70-kg adult is 350 ug/d. The intake of total chromium from food is likely to be less than that (s.3.2.1; the intake figures are most likely for adults). The fraction of Cr VI in food is likely <1 and not all of it is bioavailable. Therefore, the intake from food is less than that permitted by the RfD. The total amount ingested is, however, greater than the maximum amount allowed by the Ontario drinking water criterion. The criterion does apply strictly to intake from drinking water only. As was pointed out earlier, in calculating the RfD and the MAC, any possible intakes from food were not included. The RfD and MAC therefore represent probably the minimum intake values and represent an allowable intake on top of the intake from food.

#### Health message:

In summary, the amount of Cr VI that is ingested is less than the RfD and likely less than the intake allowed by the drinking water criterion and is in the range of recommended intakes as an essential nutrient.

#### 4.3 Dermal absorption.

The following observations and deductions can be made regarding dermal absorption:

The amounts (ug/d) of chromium, most likely in the form of Cr VI, absorbed through the skin are:

	<u>Child</u>	<u>Adult</u>
Soil and dust:	0.3 - 1.3	0.4 - 1.6
Showering/bathing	0.008 - 0.009	0.02 - 0.025
Total - ug/d	0.3 - 1.3	0.4 - 1.
ug/kg*d	0.02 - 0.08	0.006 - 0.023

#### Health message:

Compared to the RfD, these amounts are insignificant, although a strict comparison is not possible, as the RfD is set for ingested chromium and the exact gastrointestinal bioavailability is

not known.

#### 4.4 Dermatitis hazard from dermal exposure.

Only Cr VI compounds are capable of sensitizing and eliciting a reaction in sensitized individuals and only if the chromium is in solution. Sheehan *et al* (1) cite studies which show that <10% of those persons already sensitized to chromium showed an elicitation response at levels below 35 mg/L of Cr VI in solution. This is far above the levels found in drinking water. They also calculate that, assuming that only 1% of the chromium in soil is solubilised, no dermatitis should be elicited if the soil concentration is <3500 ug/g. For the sake of prudence, they reduce this to 1000 ug/g. Both of these are far above the levels found in Windsor soil.

#### Health message:

In conclusion, the potential for eliciting dermatitis appears to be negligible.

#### Summary and recommendations:

- ♦ Inhalation exposures associated with outdoor air quality (ie. 100% outdoor exposure) and with personal activity patterns exceed this chronic acceptable exposure level. Therefore, there is a possibility of long-term health effects associated with these inhalation exposures.
- ♦ The range of estimated inhalation risks associated with 'outdoor air quality' (ie. 100% outdoor exposure) is between  $3.6 \times 10^{-6}$  and  $5.5 \times 10^{-4}$ . Similarly the range of risks associated with 'typical personal exposures' is between  $1.4 \times 10^{-6}$  and  $3.0 \times 10^{-4}$ . Since these levels of risk exceed  $1 \times 10^{-5}$ , a level generally deemed to be negligible, it is recommended that chromium VI be considered a candidate for reduction of exposure.
- ♦ Exposures and therefore risks associated with 'typical personal exposures' and the risks associated with 'outdoor air quality' are similar.
- ♦ The outdoor, commuting and tobacco smoke-affected environments are the most dominant in the upper range of 'typical personal exposures'.
- ♦ The exposure that a smoker experiences is considerably higher (ie. associated risks are between  $1.4 \times 10^{-3}$  and  $1.7 \times 10^{-2}$ ) than exposures associated with 'personal activity patterns' and 'outdoor air quality'.
- ♦ Although ingestion and dermal exposures dominate over inhalation exposures for chromium, exposure via these non-inhalation routes are not associated with carcinogenic effects. Similarly, ingestion and dermal exposures are below the ingestion exposure guidelines based on chronic endpoints most appropriate for this comparison.



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## **APPENDIX 8**

### **RISK ANALYSIS FOR POLYCYCLIC AROMATIC HYDROCARBONS (PAHs)**



## APPENDIX 8

### RISK ANALYSIS FOR POLYCYCLIC AROMATIC HYDROCARBONS (PAHs)

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## POLYCYCLIC AROMATIC HYDROCARBONS (PAHs)

### DESCRIPTION and SOURCES of POLYCYCLIC AROMATIC HYDROCARBONS (PAHs).

Polycyclic aromatic hydrocarbons (PAHs), refer to a large group of chemical compounds related by their structures (ie. aromatic, 'benzene-like' rings fused together in different configurations). Although hundreds or even thousands of these compounds may exist, information is available for only a limited number. There is very limited commercial use for most of these substances. A few of them are used in medicines, and to make dyes, plastics and pesticides. They can be found in substances such as crude oil, coal tar pitch, creosote, and road and roofing tar.

PAHs are introduced into the environment via natural and anthropogenic combustion processes. Volcanic eruptions, forest and prairie fires are among the major sources of naturally produced PAHs. These natural sources make up only a minor contribution to the PAH content of air, soil, water and vegetation. Formation and release of most PAHs into the environment occurs during combustion processes. PAHs are byproducts of combustion of such materials as oil, gas, coal, wood, diesel fuel, and gasoline. Thus important sources include residential wood burning, automobile exhaust, coking (ie. steel) plants, coal tar production plants, asphalt production plants, smoke houses, aluminum production plants, coal-tarring activities and municipal trash incinerators. Improperly disposed waste from processes such as the burning of fossil fuels, refuse burning, and agricultural burning can result in site specific PAH contamination.

Everyday living can contribute many sources of PAH exposure. These include tobacco smoke, cooking meat or other food at high temperatures, which happens during grilling or charring, smoke from homes using wood as fuel for heaters and campfires, and various types of food.

PAHs always occur as complex mixtures in the environment. In the air, they generally occur adsorbed to particulates.

## 1. HAZARD IDENTIFICATION

### 1.1 Absorption and Metabolism

Polycyclic aromatic hydrocarbons (PAHs) can be absorbed following ingestion, inhalation or dermal contact. Once in the bloodstream, PAHs are quickly distributed throughout the body. Many tissues including lung, gut, kidney, and skin are able to metabolize PAHs, but liver is the predominant site of PAH metabolism<sup>23</sup>. The cytochrome P-450 family of enzymes is responsible for the initial production of epoxides from the parent PAHs. These metabolites are further processed to diols and diol-epoxides by the combined action of epoxide hydrolases and cytochrome P-450<sup>23</sup>. It is the ability of diol-epoxide metabolites to bind to DNA which is thought to be responsible for the biological activity of PAHs. Epoxides, diols, and diol-epoxides are all subject to further metabolic processing by conjugating enzymes prior to their excretion in either the bile or urine. Urinary excretion is restricted to metabolized PAHs, while small amounts of parent PAHs can be found in the bile and feces<sup>23</sup>. Excretion in the bile and feces is the primary route of PAH elimination regardless of the route of exposure.

### 1.2 Toxicology

The available literature relating the effects of acute or chronic exposure to PAHs has been extensively reviewed by the International Agency for Research on Cancer (IARC)<sup>23</sup>, and the United States Environmental Protection Agency (US EPA)<sup>24</sup>. The development of cancer appears to be the endpoint of most concern and, consequently, has received the greatest amount of attention in the literature<sup>23,24</sup>. Other

effects resulting from acute or chronic exposure to PAHs in either animals or humans have been less well studied. The reproductive and immune systems appear to be the primary targets of the non-carcinogenic effects of PAHs. Information on other acute and chronic effects is limited, and is discussed separately from the reproductive and immunotoxicity data.

Information on the effects of acute exposure to PAHs on systems other than the reproductive and immune systems is limited. The available data has been extensively reviewed by both IARC<sup>23</sup> and the US EPA<sup>24</sup>. Both IARC and the US EPA have summarized the LD<sub>50</sub> data presently available for PAHs. The LD<sub>50</sub> values are available for a limited set of PAHs which include acenaphthylene, anthracene, benzo(a)pyrene (B(a)P), carbazole, fluoranthene, phenanthrene and pyrene<sup>23,24</sup>. The LD<sub>50</sub> values are reported for a number of species and routes of exposure, however, all are in the g/kg range, varying between 250 mg/kg for B(a)P in mice to >5000 mg/kg for carbazole in rats<sup>23</sup>. Dermatological effects resulting from skin contact with PAHs have been reported for humans and animals. Dermal irritation<sup>25</sup> and increased sensitivity to ultraviolet light<sup>26</sup> have been reported in the mouse at dosages of 14 µg of B(a)P and 4 µg anthracene, respectively. Other studies report alterations in the growth of epidermal tissue and suppression of the sebaceous gland in the mouse at doses of 500 mg and 0.2 ml of B(a)P (dose unspecified), respectively<sup>27,83</sup>. However, neither of these studies provided solvent controls. Therefore, it is difficult to attribute the reported effects to B(a)P. In humans, dermally applied B(a)P was found to produce areas of hypertrophy of the papillae in all patients treated<sup>28</sup>. However, neither a total dose nor a solvent control (benzene) were provided. Therefore it is not possible, once again, to attribute the effects solely to B(a)P. A number of other effects including decreases in weight gain<sup>29</sup>, alteration in DNA turnover<sup>30,31</sup>, and hepatic and renal congestion<sup>32</sup> have also been reported at dosages that ranged between 10 mg/kg and 100 mg/kg. Excluding the reproductive and immune systems, the data suggests that the effects of acute exposure to PAHs only occur at relatively high dose levels.

For systems other than the reproductive and immune systems, there is limited data on the effects of chronic exposure to PAHs both in humans and experimental animals. The available data has been extensively reviewed by IARC<sup>23</sup> and the US EPA<sup>24</sup>. The limited data shows that chronic exposure to PAHs may produce a number of effects. The most commonly reported are decreases in both red blood cell (RBC) count and weight gain, and increases in liver weight compared to controls. In general, these effects would appear to occur only after exposure to reasonably high levels of PAH. The lowest dose at which effects were reported was 5.6 mg (total dose) for 7,12- dimethylebenz[a]anthracene (DMBA), which produced hemolymphocyte changes in the lymph nodes of rats<sup>33</sup>. Doses for other PAHs were reported to range between 15 mg/rat/day<sup>24</sup> and 2000 mg/kg/day<sup>84</sup>. Work conducted by the US EPA suggests NOAEL values in the mouse, for a number of PAHs, that range between 75 mg/kg/day (pyrene) and 125 mg/kg/day (fluoranthene, fluorene)<sup>24</sup>. In addition LOAEL values for the same compounds range between 100 mg/kg/day (acenaphthylene) and 250 mg/kg/day (fluoranthene and fluorene)<sup>24</sup>. The work of Robinson *et al.*<sup>34</sup> indicates that, in mice, the chronic effects of B(a)P may be seen at doses which are similar to those reported by the US EPA. There is insufficient data to adequately characterize the effects of chronic exposure to PAHs. However, the available data suggest that chronic effects are seen only at relatively high doses.

A number of reproductive and developmental effects including fetal malformation and mortality, tumorigenesis, immunosuppression and effects on the adult male and female reproductive systems have been reported for PAHs administered either orally or by injection<sup>35-51,85</sup>. Reproductive and developmental effects following inhalation or dermal exposure to PAHs in either humans or animals have not been reported in the literature<sup>23,24</sup>. The majority of the available studies examine the effect of PAHs exposure on fetal development<sup>35-47</sup>. Recorded effects include malformations, stillbirths, resorptions, immunosuppression, and tumorigenicity. The doses required to produce these effects are generally high and range between 1 and 200 mg/kg. In adult males, exposure to either B(a)P or 3-methylcholathrene (3-MC) has been reported to affect the tissue responsible for sperm production, thus causing sperm



abnormalities and decreases in sperm counts<sup>49</sup>. This in turn is thought to lead to decreased fertility and breeding success. In both studies, the doses required to produce these effects range between 50 and 100 mg/kg. In the female, injection of PAHs directly into the ovaries of mice resulted in oocyte destruction that ranged between 65 and 99 percent<sup>50,51</sup>. These effects were seen with a single dose (80 mg/kg) of B(a)P and 3-MC, respectively.

The effects of PAHs on the immune system were first noted by Malmgren *et al.*<sup>52</sup>, who reported reduced hemolysin titers in mice which had been treated with 3-MC, D(a,h)A, or benz(a)anthracene (B(a)A). Since this initial study, PAHs have been shown to affect a number of immune system functions in experimental animals<sup>24,52-62</sup>. Administration of a single ip injection of 3-MC to mice (dose range: 0, 0.5, 5.0, and 50 mg/kg) produced a dose dependent reduction in the lymphocyte proliferation response<sup>56</sup>. Treatment at the highest dose produced a 63 percent reduction in the proliferation response<sup>56</sup>. Mice exposed to 7,12-dimethylbenz(a)anthracene (DMBA) by sc injection (dose range: 0, 5, 50, and 100 mg/kg) showed a suppression of the lymphocyte proliferation response that ranged between 43 and 48 percent for all three doses<sup>54</sup>. Other PAHs, such as B(a)P or benzo(e)pyrene (B(e)P) do not appear to have a significant effect on this response<sup>56</sup>. However, dose-dependent reductions were reported in the binding and killing activities of splenic lymphocytes (dose range: 0, 2, 5, 10, and 50 mg/kg)<sup>56</sup>, and interleukin-2 production have been reported for mice exposed to B(a)P (dose range: 0, 5, 20, and 40 mg/kg). A number of PAHs (B(a)P, 3-MC, DMBA, DB(a,h)A) have also been shown to cause reductions in the number of plaque-forming cells and in the levels of immunoglobulins<sup>52,54,57,59,60-62</sup>. The dosages required to elicit these responses vary between PAHs but generally range between 25 and 100 mg/kg. White *et al.*<sup>61</sup> showed that a number of PAHs including B(e)P, anthracene, chrysene, perylene, phenanthrene and benzo(b)triphenylene have little or no effect on the levels of either plaque-forming cells or immunoglobulins<sup>61</sup>. The available data suggests that the effects of PAHs on the immune system are dependent on the individual PAHs as different compounds would appear to produce different responses. Unfortunately, there is insufficient data available to adequately evaluate this hypothesis. Studies have also suggested that the route of administration may play a role in the expression of the immunosuppressive effects of PAHs<sup>57,61</sup>. At present, however, there is insufficient data to evaluate this. Data which report the effects of PAH exposure on the human immune system could not be found in the literature.

The carcinogenicity and mutagenicity of individual PAHs and PAH-containing mixtures have been well studied in experimental animals<sup>63,64</sup>. Virtually no data exists on the carcinogenicity of individual PAHs in humans, and only a limited amount of data on the carcinogenicity of PAH-containing mixtures is available for humans<sup>63,64</sup>. There is evidence that a number of individual PAHs are carcinogenic in experimental animals, while others have been found to be non-carcinogenic. For other PAHs there is insufficient data to determine whether the compounds are carcinogenic or not. Because of the varying carcinogenic activities of individual PAHs it is not possible to provide a single weight of evidence carcinogenicity assessment for PAHs as a class. The carcinogenicity of each PAH must be assessed separately. A list of PAHs for which weight-of-evidence carcinogenicity assessments are available are shown in Table A. While it is not possible to provide a carcinogenicity assessment for PAHs as a class, it may be possible to assign such a carcinogenicity assessment to PAH-containing complex mixtures on the basis of weight of evidence. A list of PAH-containing complex mixtures for which weight-of-evidence carcinogenicity assessments are available are shown in table A.

The assessment of PAHs carcinogenicity is further complicated by the dependence of tumor type and location on species and route of administration. Administration of 3-MC to the respiratory tract in mice produces primarily pulmonary adenomas. Squamous cell carcinomas have also been reported, but only at relatively high doses (3mg 3-MC/mouse)<sup>65</sup>. In rats, treatment with 3-MC (3 mg/rat) produced squamous cell carcinomas, while adenomas were virtually absent<sup>66</sup>. Topical applications of DMBA, B(a)P or 3-MC tends to produce squamous cell carcinomas in mice and rats<sup>67</sup>. In hamsters, topical applications of DMBA produces melanomas rather than squamous cell carcinomas, while B(a)P and 3-MC do not

appear to produce tumors<sup>67</sup>. For some carcinogenic PAHs it has been shown that the route of administration has an effect on the type of tumor formed and upon its location<sup>68</sup>. Administration of PAHs to either the respiratory tract or the skin tends to form tumors at the site of initial contact. Oral exposure to PAHs tend to produce tumors at sites removed from the initial point of contact<sup>68</sup>. Thus not only must the carcinogenic action be evaluated, but the route of administration and the species studied must also be considered when assessing the carcinogenicity of each PAH.

**Table A: Weight of Evidence Carcinogenicity Assessment for Individual PAH.**

NAME	CARCINOGENICITY ASSESSMENT		NAME	CARCINOGENICITY ASSESSMENT	
	IARC <sup>1</sup>	USEPA <sup>2</sup>		IARC <sup>1</sup>	USEPA <sup>2</sup>
Acenaphthene, 5-nitro-,	2B		Coronene	3	
Acenaphthylene		D	Cyclopenta[cd]pyrene	3	
Anthanthrene	3		Dibenz[a,h]acridine	2B	
Anthracene	3	D	Dibenz[a,j]acridine	2B	
Anthracene, 9-nitro-,	3		Dibenz[a,c]anthracene	3	
Benz[a]acridine	3		Dibenz[a,h]anthracene	2A	B2
Benz[a]anthracene	2A	B2	Dibenz[a,j]anthracene	3	
Benzo[a]pyrene	2A	B2	7H-dibenzo[c,g]carbazole	2B	
Benzo[b]fluoranthene	2B	B2	Dibenzo[a,e]fluoranthene	3	
Benzo[c]phenanthrene	3		Dibenzo[h,rst]pentaphene	3	
Benzo[e]pyrene	3		Dibenzo[a,e]pyrene	2B	
Benzo[ghi]fluoranthene	3		Dibenzo[a,h]pyrene	2B	
Benzo[ghi]perylene		D	Dibenzo[a,il]pyrene	2B	
Benzo[j]fluoranthene	2B		Dibenzo[a,l]pyrene	2B	
Benzo[k]fluoranthene	2B	B2	Fluoranthene	3	D
Benzo[a]fluorene	3		Fluoranthene, 2-methyl-,	3	
Benzo[b]fluorene	3		Fluoranthene, 3-methyl-,	3	
Benzo[c]fluorene	3		Fluoranthene, 3-nitro-,	3	
Carbazole	3		Fluorene	3	D
Chrysene, 1-methyl-,	3		Indeno[1,2,3-cd]pyrene	2B	B2
Chrysene, 2-methyl-,	3		Phenanthrene	3	D
Chrysene, 3-methyl-,	3		Phenanthrene, 1,4-dimethyl-,	3	
Chrysene, 4-methyl-,	3		Perylene	3	
Chrysene, 5-methyl-,	2B		Pyrene	3	D
Chrysene, 6-methyl-,	3		Pyrene, 1-nitro-,	3	
Chrysene, 6-nitro-,	3		Pyrene, 1,8-dinitro-,	3	
Chrysene	3	B2	Quinoline, 8-hydroxy-,	3	



#### 1 IARC 1987 classification scheme

- 1 - carcinogenic to humans (There is sufficient evidence for carcinogenicity in humans)
- 2A - probably carcinogenic to humans (There is limited evidence for carcinogenicity in humans and sufficient evidence for carcinogenicity in experimental animals strengthened by supporting evidence from other relevant data)
- 2B - possibly carcinogenic to humans (There is limited evidence for carcinogenicity in humans in the absence of sufficient evidence for carcinogenicity in experimental animals. It may be used when there is inadequate evidence of carcinogenicity in humans or when human data are nonexistent but there is sufficient evidence in experimental animals. In some instances, an agent for which there is inadequate evidence or no data in humans but limited evidence of carcinogenicity in experimental animals together with supporting evidence from other relevant data may be placed in this group).
- 3 - not classifiable as to carcinogenicity in humans
- 4 - probably not carcinogenic to humans (there is evidence suggesting lack of carcinogenicity in humans together with evidence suggesting lack of carcinogenicity in experimental animals. In some circumstances, agents for which there is inadequate evidence or no data on carcinogenicity in humans but evidence suggesting lack of carcinogenicity in experimental animals, consistently and strongly supported by a broad range of other relevant data, may be classified in this group).

#### 2 USEPA, 1991 classification

- B2 - probable human carcinogen
- D - not classifiable as to human carcinogenicity

Table A (cont): Weight of Evidence Carcinogenicity Assessments for PAH containing Mixtures

NAME	IARC
Bitumens	3
- extracts of air or steam refined	2B
Carbon blacks	3
Coal gasification	1
Coal-tar pitches	1
Coal-tars	1
Coke production	1
Creosotes	2A
Iron and steel founding	1
Soots	1
Tobacco smoke	1

## 2. DOSE-RESPONSE INFORMATION/CURRENT EXPOSURE GUIDELINES

### 2.1 The Relative Potency Factor (RPF) Approach in the Assessment of the Carcinogenicity of Environmental Mixtures of PAHs

Numerous uncertainties surround the assessment of the potential health effects of PAHs on communities. This class of compounds has been extensively investigated because of its potential adverse health effects, its ubiquity in the various environmental compartments, and because of the inherent difficulties encountered by regulators in assessing the toxicologic effects of these variable, complex mixtures. The latter is particularly important in the current context as little is known on the precise qualitative and quantitative outcome that may be produced by different PAH mixtures in both animals and humans. Furthermore, extrapolation of experimental and epidemiologic observations obtained with mixtures of fairly known composition, to the general human situation is highly uncertain in view of the diversity of mixture profiles to which humans are exposed in the environment. In order to circumvent these difficulties and to provide a manageable approach to estimate the carcinogenic potency of PAH mixtures, several authors have used the concept of the Relative Potency Factor (RPF), also known as the Toxic Equivalency Factor (TEF).

The RPF methodology is based on the premise that the individual PAHs composing a given mixture act additively in the same target organ (e.g., respiratory tract), through the same mechanistic pathway (e.g., bioactivation to a diol-epoxide which subsequently binds to critical DNA sites), and induce a similar toxicologic effect (e.g., a given type of tumor, although in this case total cancer incidence is the critical endpoint). Therefore, under these assumptions the only variable differentiating the various PAHs is their potency, i.e., their efficiency, relative to a reference PAH, to induce cancer. Benzo(a)pyrene (B(a)P) is generally used as the reference PAH (RPF = 1) to which other PAHs are quantitatively compared, in view of its extensive data-base of effects on biological systems and the availability of adequate carcinogenicity data for dose-response assessment. Other PAHs RPFs are generally calculated based on studies which have measured side-by-side with B(a)P, and in the same assay system, the occurrence of the toxicological end-point of interest. The final product of the RPF methodology is a value which expresses the potency of the PAH mixture as B(a)P equivalents, i.e.,  $B(a)P_{eq} = \{(PAH_1 \times RPF_1) + (PAH_2 \times RPF_2) + \dots (PAH_n \times RPF_n)\}$ , where  $PAH_n$  is the concentration of nth PAH in the mixture, and  $RPF_n$  is its potency factor relative to B(a)P. The adoption of this concept by various investigators has resulted in the generation of several scales of RPFs for a limited number of carcinogenic PAHs<sup>1-6</sup> (Table 2.1).

Despite the immediate utility of the RPF methodology for regulatory control and enforcement, several conceptual factors render this approach uncertain and, thus, provisional. These uncertainties are mainly related to the general issue of how to assess the toxicology of carcinogenic mixtures (e.g., in the presence of potentiation, synergism, promotional and cocarcinogenic effects), to the database used to derive RPFs (e.g., application of RPFs based on skin painting studies to oral and pulmonary exposures), and to the application of the RPFs to different exposure scenarios (e.g., RPFs may change as a function of the dose, i.e., be pharmacokinetics-dependent). Furthermore, derivation of RPFs is possible only for a few PAHs and, therefore, the methodology ignores numerous other compounds contained in these mixtures. As a result, it is uncertain whether application of these RPFs may be representative of the effects induced by exposure to the whole mixture.

Although a number of RPF schemes are available in the literature (see table 2.1), direct comparison between these studies is difficult. As can be seen from the data in table 2.1, reported values can vary by over two orders of magnitude (chrysene 0.001 - 0.26). There are a number of potential sources of the variation including; the use of different species and strains of animals, differences in the route of administration and treatment protocols and differences in the mathematical models used to estimate potencies. While these factors can effect the determination of RPF values, RPF schemes can be compared

and combined to produce a composite scheme. However, this requires that there be a demonstrable level of agreement in RPF values between studies (i.e., that the RPF values for compounds common to all studies should not vary significantly between studies). A large overlap in the compounds tested and a good agreement in the RPF values reported between studies, would suggest that the data sets are comparable and could be combined. If, however, there is little overlap in the compounds tested and if there is poor agreement between the reported RPF values, it would indicate that the data sets are not comparable and should not be combined. There are only three compounds which are common to all the cited papers; B[a]P, benzo[b] fluoranthene (B[b]F) and indeno[1,2,3-cd]pyrene (IP). Reported RPF values for B[b]F range between 0.02 and 0.14, while those for IP lie between 0.006 and 0.28. This large range for IP suggests that the agreement between data sets is poor. Varying degrees of agreement can be seen with other compounds listed. This also suggests that the agreement between data sets is poor and that the RPF values from a single study should be selected.

Table 2.1. Relative Potency Factor (RPF) Scales Proposed by Various Investigators<sup>1-6</sup>

PAH	RPF					
	Willes 1992 <sup>2</sup>	Nesbit 1992 <sup>1</sup>	Thorslund 1990 <sup>3</sup>	Rugen 1989 <sup>4</sup>	Krewski 1989 <sup>5</sup>	Chu 1984 <sup>6</sup>
anthanthrene	NDA	NDA	0.32	NDA	0.320	NDA
benzo(a)pyrene	1.0	1.0	1.0	1.0	1.0	1.0
benzo(e)pyrene	0.05	NDA	NDA	NDA	0.004	NDA
benzo(a)anthracene	0.033	0.1	NDA	0.006	0.145	0.013
benzo(b)fluoranthene	0.1	0.1	0.1228	0.02	0.14	0.08
benzo(j)fluoranthene	NDA	NDA	.0523	0.076	0.061	NDA
benzo(k)fluoranthene	0.01	0.1	0.0532	NDA	0.066	0.004
benzo(g,h,i)perylene	1.0	0.01	0.0212	NDA	0.022	NDA
chrysene	0.26	0.01	NDA	NDA	0.0044	0.001
dibenzo(a,h)anthracene	1.4	5	NDA	0.6	1.11	0.69
fluoranthene	0.034	0.001	NDA	NDA	NDA	NDA
indeno(1,2,3-c,d)pyrene	0.1	0.1	0.278	0.006	0.232	0.017
pyrene	NDA	0.001	NDA	NDA	0.081	NDA

<sup>1</sup> RPF for the nth PAH was calculated from the Rugen *et al.* data as the  $AEL_{B[a]P}/AEL_n$  ratio, where AEL is the Acceptable Exposure Level for drinking water derived by these authors.

When selecting RPF values from a single study, some consideration must be given to the quality of the data used to derive the RPF values. Studies which derive RPF values for multiple PAH using a single



species/strain, test protocol and mathematical model greatly reduce the number of experimental variables. This increases the likelihood that observed differences are due to differences in PAH potencies and not other factors. Studies of this nature provide the best RPF schemes. Of the cited studies, only the one by Thorslund<sup>3</sup> falls into this category. Other studies<sup>1,5</sup> use data from various sources to develop RPF schemes. While these RPF schemes have a greater level of experimental variation, efforts are made to determine the level of agreement between data sets by comparing only relative potencies and not absolute potencies, and by ensuring that there is a reasonable overlap in the tested compounds between studies. Other studies develop RPF schemes from multiple papers using relative potencies where B[a]P is the only compound common to all studies<sup>4</sup>, while other studies develop RPF schemes using absolute potencies from various sources<sup>2</sup>. These latter types of studies have greater potential to introduce experimental error into the RPF schemes than those discussed previously. Therefore, if better studies (those which introduce less experimental variation) are available, they should be given preference.

In the final selection of an RPF scheme, consideration must be given not only to the quality of the data available, but also to the intended use of the data. In this report, the intent is to use available RPF values to estimate cancer risk for a number of PAH (18 in total). Therefore, the best data set would be one which provides RPF values for as many of these 18 as possible. As discussed above, the RPF values reported by Thorslund<sup>3</sup> are the most likely to have the smallest amount of associated experimental error. However, this study provides RPF values for only 7 of the 18 compounds listed, thereby leaving 11 compounds for which RPF values are not available. Consequently, the errors associated with extrapolating from these 7 compounds to the full 18 is liable to be reasonably large. The RPF values reported by Krewski *et al.*<sup>5</sup>, while subject to a greater degree of experimental variation than that of Thorslund<sup>2</sup>, covers 12 of the 18 compounds of interest. Therefore, the levels of extrapolation required in subsequent sections will be less than that required if the Thorslund data set was selected. The remaining data sets provide RPF values for fewer PAH and are prone to greater levels of experimental error than either the Thorslund or Krewski schemes. Based on these considerations, the decision was made to use the RPF values reported by Krewski *et al.*<sup>5</sup> in subsequent sections of the document.

In order to utilize the RPF methodology in the present study to assess the potential health impact of PAHs present in the Windsor airshed, information related to the carcinogenic potency of the reference PAH B(a)P is introduced in the next section, while potential exposures and the risk characterization are presented in sections 3 and 4, respectively.

## 2.2 Air Guidelines

### 2.2.1 Chronic, Non-Carcinogenic Effects

No Reference Concentration (RfC) for effects other than cancer induced by B(a)P is proposed in the US EPA Integrated Risk Information System (IRIS)<sup>7</sup>, and in the Health Effects Assessment Summary Tables (HEAST)<sup>8</sup>. EPA defines an RfC as an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime.

Similarly, no Acceptable Exposure Levels (AEL), no Annual Guideline Concentration (AGC), and no Threshold Effect Exposure Limit (TEL) for non-cancer, chronic health effects have been reported, respectively, by the California Air Pollution Control Officer Association (CAPCOA) in their 1992 Risk Assessment Guidelines<sup>9</sup>, by the New York State Department of Environmental Conservation (NYSDEC) in their Air Guide-1<sup>10</sup>, and by the Massachusetts Department of Environmental Protection (MDEP) in their Health Effect Assessment Methodology guidelines<sup>11</sup>.

The World Health Organization, in their Air Quality Guidelines for Europe<sup>13</sup> states that owing to its carcinogenicity, no safe level of PAHs can be recommended.

Generally, the inhalation chronic AEL, TEL, AGC, and the inhalation RfC noted above are comparable in their use for assessing chronic effects (except carcinogenic effects) due to inhalation. It is expected that constraining environmental exposures of human populations to cancer-preventive levels of B(a)P should decrease to negligible levels, or simply eliminate depending on the end-point of concern, the probability of occurrence of chronic non-cancer health effects.

## 2.2.2 Carcinogenic effects

Contrary to systemic, non-carcinogenic health effects, several attempts have been made to propose a unit risk factor for inhaled B(a)P. However, fundamental problems are also associated with these approaches, which partly explains the lack of consensus among investigators who have addressed this issue. Major uncertainties include 1) the questionable quality of the available database (e.g., protocol deficiencies); 2) the different interpretations of experimental data provided by different investigators; and 3) uncertainties associated with the extrapolation of bioassay results obtained with animals exposed to the pure B(a)P, to situations where individuals are environmentally exposed to particle-bound B(a)P, thus resulting in different pattern of deposition and, hence, bioavailability in the pulmonary tract. It should be kept in mind, therefore, that no one approach is completely satisfactory, and that application of the available unit risk or potency slope factors derived from animal bioassays to environmental exposure scenarios requires consideration of particle characteristics and the associated lung dosimetry.

It is also important to note that unit risk factors presently available from some jurisdictions have been converted directly from the oral slope factor obtained from oral feeding studies in rodents. Conceptually, this approach is not recommended in view of the tumorigenicity of B(a)P at the site of injection (i.e., respiratory tract and upper digestive tract tumors following inhalation and oral exposure, respectively) which are used to model the dose-response relationship.

For the purpose of estimating cancer risk, the U.S. EPA<sup>8,15</sup> has established in the past an *inhalation* slope factor of  $6.1 \text{ (mg/kg-day)}^{-1}$ , corresponding to an inhalation unit risk factor of  $1.7 \times 10^{-3} \text{ (ug/m}^3\text{)}^{-1}$ . These values were derived based on the incidence of respiratory tract tumors resulting from inhalation exposure of hamsters to a saline solution of B(a)P, and by considering an inhalation rate of  $0.037 \text{ m}^3/\text{day}$ , a standard body weight of  $0.12 \text{ kg}$ , and 100% absorption<sup>14</sup>. This value, however, has been withdrawn from the IRIS database and, presently, no value for the inhalation route is available. Reasons for this withdrawal included the use of inappropriate assumptions for animal lifespan and breathing rates, incorrect exposure values, and neglect of some relevant data from the original study regarding surviving data and exposure data for the highest exposure level. According to a recent study by the California Department of Health Services (CDHS)<sup>14</sup>, changing both the inhalation rate and body weight within a range considered biologically acceptable for hamsters results in unit risk factors varying from  $1.1 \times 10^{-3}$  to  $3.7 \times 10^{-4} \text{ (ug/m}^3\text{)}^{-1}$ , i.e., variations are less than 40% of the original EPA value.

The California Air Pollution Control Officers Association (CAPCOA), in their recent Risk Assessment Guidelines<sup>9</sup>, and the New Jersey Department of Environmental Protection and Energy<sup>21</sup>, have both suggested a unit risk factor of  $1.7 \times 10^{-3} \text{ (ug/m}^3\text{)}^{-1}$  based on the US EPA methodology.

A unit risk factor of  $5 \times 10^{-4} \text{ (ug/m}^3\text{)}^{-1}$  has been proposed by the New York State Department of Health (NYSDOH) and used by the New York State Department of Environmental Conservation (NYSDCE)<sup>10</sup> to calculate an Annual Guideline Concentration (AGC) of  $2 \times 10^{-3} \text{ ug/m}^3$ , corresponding to an excess lifetime cancer risk of  $1/10^6$ .



On the other hand, few other US state jurisdictions have developed unit risk or inhalation potency factors, despite the fact that, in several instances, Acceptable Ambient Concentrations or Guidelines (AAC/G) have been proposed<sup>16</sup>. Hence, for the states of Vermont, Florida, Kansas, Texas, and North Carolina an annual AAC/G of  $3 \times 10^{-3}$  ug/m<sup>3</sup> is reported in the most recent NATICH<sup>16</sup> database, while an annual value of  $7 \times 10^{-4}$  ug/m<sup>3</sup> is reported for the state of Pennsylvania. Because information regarding the methodology used by these jurisdictions was not available (i.e., choice of critical studies, statistical treatment of data, mathematical modeling of the dose-response, and acceptable lifetime excess cancer risk), it is not possible to derive the corresponding unit risk factors. Other jurisdictions, such as the State of Massachusetts, have not proposed permissible ambient values for B(a)P and other PAHs.

The World Health Organization, in its Air Quality Guidelines for Europe<sup>13</sup> states that owing to its carcinogenicity, no safe level of B(a)P or PAHs can be recommended.

An Ambient Air Quality Concentration (AAQC) of  $1.1 \times 10^{-3}$  ug/m<sup>3</sup> was proposed, in 1986, by the Ontario Ministry of Labour (OMOL), and implemented by the Ontario Ministry of the Environment (OMOE). The OMOL rationale was based on one of the four potency factors originally developed by the US EPA, as modeled for an excess lifetime cancer risk of  $1/10^6$  with a linearized multistage model. Consequently, a unit risk factor of  $9.1 \times 10^{-4}$  (ug/m<sup>3</sup>)<sup>-1</sup> can be derived.

Unit risk and/or potency slope factors have also been proposed by independent investigators who have reevaluated the available biomedical data on B(a)P. Hence, in a report completed by Clements Associates Inc.<sup>17</sup> and submitted to the US EPA, the authors propose an inhalation potency factor of 0.136 (mg/kg-day)<sup>-1</sup>. This value was based strictly on an alternative interpretation of the pathology, exposure, and survival data of an inhalation bioassay conducted in rodents which partly served as a basis to the former US EPA inhalation potency factor. Furthermore, a two-stage model with exponential expansion of a population of preneoplastic cells was adopted as an alternative to the classical linearized multistage model. More recently, Willes *et al.*<sup>2</sup> have reported a Risk Specific Dose (RsD) of 0.0037 ug B(a)P/kg-day at a specific risk level of  $1/10^5$ , thus corresponding to a potency slope factor of  $2.7 \times 10^{-3}$  ug/kg-day. This value, was based on a combination of bioassay data from inhalation and intratracheal exposure in rodents with the application of the linearized multistage model.

Finally, in some instances study groups have attempted to derive unit risk and/or slope potency factors from epidemiological data based on the exposure of workers to different processes of coal combustion and exposure of women cooking over smoky coal in indoor environments<sup>18</sup>. The mixtures associated with these processes are known to present substantial qualitative and quantitative differences from environmental mixtures and, thus, the relevance of applying the associated unit risk or potency factors to public health issues is uncertain. Furthermore, the cancer potency of these mixtures is based on the effects of total PAHs (and other human carcinogens such as nitrosamines), as compared with the RPF approach which is based on B(a)P and a few selected PAHs. Because of these reasons, epidemiological data-based potency factors, derived from and applied to whole PAH mixtures (ie. mixtures whose relevance to urban environmental PAH mixtures is uncertain) will not be utilized in this study.

Few occupational exposure guidelines have been developed for B(a)P and those available are not considered protective enough. In the U.S., the Permissible Exposure Limit (PEL), established by the Occupational Safety and Health Administration (OSHA)<sup>19</sup> is 0.2 mg/m<sup>3</sup>. The American Conference of Governmental Industrial Hygienists (ACGIH)<sup>19</sup> presently has no Threshold Limit Value-Time Weighted Average (TLV-TWA), although B(a)P has been designated as an A2 carcinogen (ie. suspected human carcinogen), by the TLV Committee. The National Institute of Occupational Safety and Health (NIOSH)<sup>19</sup> has recommended a REL-TWA of 0.1 mg/m<sup>3</sup>.

Presently, no occupational guideline for benzo(a)pyrene in Ontario is available, and no value has been

proposed in the recent review of five jurisdictions which serves as a basis for the development of new occupational standards<sup>20</sup>.

The above guidelines for atmospheric benzo(a)pyrene are summarized in Table 1. below.

### 2.3 Other Route Guidelines

There appear to be no human studies regarding cancer effects after oral exposure to B(a)P. Rodents fed B(a)P have developed tumors in the upper digestive tract, but also at distant sites, thus indicating the systemic toxicity of B(a)P. It is generally assumed, in the context of guideline development, that humans also will develop tumors if B(a)P is ingested.

For the purpose of estimating cancer risk from oral exposures, the US EPA<sup>7,16</sup> has established an oral slope factor of  $5.8 \text{ (mg/kg-day)}^{-1}$ . The oral slope factor was derived based on a geometric mean of four slope factors obtained by different modeling procedures, and from the combination of multiple data sets from two different reports using more than one sex and species. The critical end-point used by the US EPA was the incidence of squamous cell papillomas and carcinomas observed in the forestomach of mice chronically fed with B(a)P through their diet. As mentioned in the preceding sections, it is not recommended to estimate a unit risk factor for inhalation exposure, from the oral slope factor in view of the portal-of-entry effects induced by B(a)P.

The current US EPA oral slope factor replaces the former value of  $11.53 \text{ (mg/kg-day)}^{-1}$  derived with only one set of data, and modeled with the classical linearized multistage model<sup>14,15</sup>. This value of  $11.53 \text{ (mg/kg-day)}^{-1}$ , however, is still being used by some jurisdictions and/or regulatory agencies, including California CAPCOA in their 1992 Air Toxics "Hot Spots" Program, Risk Assessment Guidelines<sup>9</sup>. No other information regarding oral potency factors for B(a)P could be located in the open literature.

The US EPA issued drinking water health guidelines for B(a)P<sup>7</sup>. Hence, the Maximum Contaminant Level Goal (MCLG) and the Maximum Contaminant Level (MCL) proposed in 1990 are 0 mg/L and 0.0002 mg/L, respectively. Contrary to the MCLG, the MCL considers economic and technological feasibility.

The current Maximum Allowable Concentration (MAC) for drinking water recommended in the Canadian Drinking Water Guidelines<sup>22</sup> is 0.01 ug/L. This value was derived based on the incidence of stomach tumors in mice following exposure through the diet, as modelled with the linearized multistage model. The corresponding unit risk factor was  $5 \times 10^{-5} \text{ (ug/L)}^{-1}$ . From this information, it can be deduced that a lifetime excess cancer risk of  $1/10^6$  would be associated with the ingestion of water containing 0.02 ug B(a)P/L, and that the corresponding oral slope factor would be  $2.3 \text{ (mg/kg-day)}^{-1}$ .

The above ingestion guidelines are summarized in Table 1.

TABLE 1. Summary of Exposure Guidelines for Benzo(a)pyrene from Leading Agencies

GUIDELINE APPLICATION	AGENCY(IES)	ORIGINAL VALUE	CONCENTRATION ("Original Form" converted to these -as applicable)			CALCULATED "ALLOWABLE" INTAKE (3)
			Unit Risk (1)	R <sub>s</sub> C (2) (1 x 10 <sup>-5</sup> )	R <sub>s</sub> C (2) (1 x 10 <sup>-4</sup> )	
INHALATION GUIDELINES						
Occupational	OSHA, NIOSH	100 - 200 ug/m <sup>3</sup>	NA	NA	NA	2000000 - 4000000 (2.9 x 10 <sup>-5</sup> - 5.7 x 10 <sup>-3</sup> )
Ambient Air Quality Guidelines	US states	7 X 10 <sup>-4</sup> - 2 X 10 <sup>-3</sup> ug/m <sup>3</sup>	NA	NA	NA	14 - 40 (2 x 10 <sup>-2</sup> - 5.7 x 10 <sup>-2</sup> )
Ontario Air Quality Guideline	OMOL/OMOE	1.1 X 10 <sup>-3</sup> ug/m <sup>3</sup>	-	-	-	22 (3.1 x 10 <sup>-2</sup> )
Chronic AELs/RfCs	-	-	-	-	-	-
Inhalation Cancer Potency Factor	CAPCOA, NJDEP NYSDOH	See Unit Risk column	1.7 X 10 <sup>-3</sup> 5 X 10 <sup>-4</sup>	5.9 X 10 <sup>-3</sup> 0.02	5.9 X 10 <sup>-4</sup> 0.002	for 1 x 10 <sup>-5</sup> risk: 120 - 400 (1.7 x 10 <sup>-4</sup> - 5.7 x 10 <sup>-4</sup> ) for 1 x 10 <sup>-4</sup> risk: 12 - 40 (1.7 x 10 <sup>-2</sup> - 5.7 x 10 <sup>-2</sup> )
INGESTION GUIDELINES						
Drinking Water Guideline	US EPA MCL Canadian MAC	0.2 ug/L 0.01 ug/L	NA	NA	NA	15 - 300 (2.1 x 10 <sup>-2</sup> - 4.3 x 10 <sup>-1</sup> )
Oral Cancer Potency Factor	US EPA CAPCOA	See Unit Risk column	5.8 11.5 (mg/kg-day) <sup>1</sup>	8 X 10 <sup>2</sup> 4 X 10 <sup>2</sup>	8 X 10 <sup>3</sup> 4 X 10 <sup>3</sup>	for 1 x 10 <sup>-5</sup> risk: 60 - 120 (8.6 x 10 <sup>-2</sup> - 1.7 X 10 <sup>-1</sup> ) for 1 x 10 <sup>-4</sup> risk: 6 - 12 (8.6 x 10 <sup>-1</sup> - 1.7 X 10 <sup>-1</sup> )

<sup>1</sup>For inhalation and ingestion guidelines, unit risks are expressed as (ug/m<sup>3</sup>)<sup>-1</sup> and (ug/L)<sup>-1</sup>, respectively

<sup>2</sup>For inhalation and ingestion guidelines, risk specific concentrations are expressed as ug/m<sup>3</sup> and ug/L, respectively

<sup>3</sup>Intake was computed by assuming, where applicable, an adult weight of 70 kg, a breathing rate of 20 m<sup>3</sup>/day, a water intake of 1.5 L/day. In all cases 100% bioavailability of the intake was assumed.



### 3. HUMAN EXPOSURE ASSESSMENT

#### 3.1 Inhalation

##### 3.1.1 Ambient Air Quality

Ambient levels of PAHs have been measured at five fixed site stations in Windsor by two monitoring agencies, the Ontario Ministry of Environment and Energy and, the Environmental Protection Service of Environment Canada<sup>12</sup>. The measurements include five years of data and 444 samples, each collected over a 24 hour period. Since the status of the Detroit coke oven operations changed during this study, data from all the monitoring stations further inside Windsor, further away from the direct impact of the coke ovens, were utilized. Data from these stations were deemed to be more representative of long-term concentrations in the Windsor airshed, spanning the time before and after the change in coke oven operations.

As noted before, PAHs in the environment, including air, occur as mixtures. The monitoring methodology attempts to measure the concentration of as many individual PAH compounds as possible. None of the presently available methodologies measure all the individual PAHs that may be in the air, because of sampling or analytical methodology constraints. Furthermore, some of the measured PAHs are considered carcinogens, some non-carcinogens and some cannot be classified regarding carcinogenicity by regulatory agencies. Because of these monitoring limitations, the fact that one is dealing with mixtures and also dealing with substances of different levels of carcinogenicity various approaches can be and have been used to assess the impact of PAHs in air, as well as, in other media.

Air concentrations of PAHs will be discussed and presented, using two different approaches. Briefly, these are:

(1) Expressing the measurements in terms of Benzo(a)Pyrene (ie. B(a)P) toxic equivalents using relative potency factors (RPFs), also called toxic equivalent factors (TEFs). This yields an estimated concentration of the mixture in terms of B(a)P, taking into account PAHs classed as carcinogens and also some PAHs whose carcinogenicity has not been unequivocally demonstrated (see Table A, sect. 1.2) but for which TEFs have been proposed in the literature. Measured PAHs, for which TEFs (or RPFs) have been proposed by Krewski et. al.<sup>5</sup> (ie. the set of TEFs selected for this study), as discussed in section 2.1 and Table 'B', will have the TEFs applied to calculate B(a)P equivalents. Measured PAHs, for which TEFs have not been proposed in the literature, will not be addressed in this approach.

(2) Using the measured concentrations of B(a)P directly. Some authors<sup>70</sup> have used B(a)P measurements to estimate the 'total carcinogenic PAHs' that could be in the air, by multiplying the B(a)P concentrations by 10 to estimate the 'total carcinogenic PAHs'.

Some of the reasons behind this approach include the following. Studies<sup>70</sup> indicated that B(a)P comprises between 5% and 30% of carcinogenic PAHs in outdoor air, Menzie et. al.<sup>70</sup> have selected a value of 10% (ie. multiplying B(a)P concentrations by 10) to estimate carcinogenic PAHs in air. Other studies (Grimmer<sup>69</sup>) have indicated that B(a)P contributes 10-11% (ie.  $\approx 1/10$ th) to the total carcinogenicity of various PAH containing emissions. Studies of Grimmer<sup>69</sup> have also shown that the carcinogenicity of PAH mixtures resides primarily with PAHs having greater than 3 rings. All of the measured PAHs in Table 2.a. have greater than 3 rings. Also, some of the measured PAHs in Table 2.b have either not been examined and classified or, were not classified unequivocally regarding their carcinogenicity by IARC and EPA (see Table A, section 1.2). For the above reasons and recognizing that the measurement process does not

account for all PAHs that may be in the air, this approach of multiplying B(a)P concentrations by ten can be considered prudent and responsible.

These approaches should yield a range of estimated intakes, allow for comparison of inhalation exposures to exposures from other media, allow comparison to B(a)P guidelines (ie. generally guidelines for only B(a)P are available) and allow estimation of risks in various ways (ie. in section 4).

It is possible to estimate the daily intake of PAHs associated with the above two measures (ie. approaches 1. and 2. above) of Windsor ambient air quality, recognizing that personal real exposures/intakes may be quite different as further discussed in section 3.1.2. The above two approaches are summarized in Tables 2.a and 2.b respectively. Further explanatory notes on the two approaches can be found in the footnotes of these two tables. Tables 2.a and 2.b show the estimated intakes for two different receptors, *i.e.*, an adult and a child. It should be noted that these intakes were calculated based on 24 hour exposures and assume 100% bioavailability by the inhalation route.



Table 2.a. Estimated Daily Intakes of PAHs Associated with Ambient Air Quality in Windsor - Expressed as B(a)P Equivalents

PAH	CONCENTRATION Lowest mean // Highest 90th percentile (a) ng/m <sup>3</sup>	Toxic Equivalent Factor (TEF) (c)	B(a)P Equivalent Concentration L. Mean // H. 90th perc. ng B(a)P Eq./m <sup>3</sup>	TOTAL B(a)P Eq. L. Mean // H. 90th perc. ng B(a)P Eq./m <sup>3</sup>	Adult (f) L. Mean // H. 90th ng B(a)P Eq./day (ng/kg-day)	Child (f) L. Mean // H. 90th ng B(a)P Eq./day (ng/kg-day)
Fluoranthene	4.24 // 18.8	-	-			
Pyrene	2.96 // 13.02	0.081	0.24 // 1.1			
Benzo(a)Fluorene	0.11 // 1.79	-				
Benzo(b)Fluorene	0.37 // 1.16	-	-			
1-Me-Pyrene	0.18 // 0.60	-	-			
Benzo(g,h,i)Fluoranthene	0.43 // 1.27	-	-			
Benz(a)Anthracene	0.16 // 1.50	0.145	0.02 // 0.22			
Chrysene & Triphenylene <sup>b</sup>	0.63 // 3.38	0.0044	0.003 // 0.01			
Benzo(b)Fluoranthene <sup>d</sup>	0.8 // 3.5	0.14	0.11 // 0.49	0.68 // 3.7	13.6 // 74 (0.19 // 1.1)	3.4 // 18.5 (0.2 // 1.2)
Benzo(k)Fluoranthene <sup>d</sup>	0.3 // 1.3	0.066	0.02 // 0.09			
Benzo(e)Pyrene	0.44 // 1.54	0.004	0.02 // 0.006			
Benzo(a)Pyrene	0.16 // 1.14	1.0	0.16 // 1.14			
Perylene	0.08 // 0.24	-	-			
Indeno(1,2,3-cd)Pyrene	0.26 // 1.71	0.232	0.06 // 0.4			
Dibenz(ah)Anthracene	0.03 // 0.08	1.11	0.03 // 0.09			
Benzo(b)Chrysene <sup>c</sup>	0.13(min) // 0.38(max)	-	-			
Benzo(g,h,i)Perylene	0.28 // 1.58	0.022	0.006 // 0.03			
Anthracene	0.03 // 0.09	0.32	0.01 // 0.03			

- a) The first value is the lowest mean concentration from the five Windsor sites; the second value is the highest 90th percentile concentration from the five Windsor sites; total number of 24 hr average samples is 444;
- b) It was assumed that all of the coeluting substance was chrysene;
- c) For Benzo(b)chrysene the minimum and maximum concentrations were used since only these were available;
- d) Environment Canada reports Benzo(b)fluoranthene and Benzo(k)fluoranthene together; MOEE reports them separately; the average MOEE % distribution was used to estimate separate concentrations for these substances from EPS data (ie. B(k)F is  $\approx 27\%$  of the total of B(b)F + B(k)F)
- e) TEQ values taken from Krewski<sup>1</sup>(see section 2.1)
- f) Assuming the following weights and inhalation rates per day (ie. per 24 hour period):  
 Adult: 70 kg; 20 m<sup>3</sup>/day  
 Child: 15 kg; 5 m<sup>3</sup>/day

Table 2.b. Estimated Daily Intakes of B(a)P and 'Total Carcinogenic PAH' Associated With Ambient Air Quality in Windsor

B(a)P CONCENTRATION(a)  Lowest Means // ? Highest 90th percentile  ng/m <sup>3</sup>	Adult (c)	Child (c)
	L. Mean // H. 90th perc.  ng/day (ng/kg-day)	L. Mean // H. 90th perc.  ng/day (ng/kg-day)
0.16 // 1.14	B(a)P INTAKE	
	3.2 // 22.8 (0.05 // 0.3)	0.8 // 5.7 (0.05 // 0.4)
	'Total Carcinogenic PAH' INTAKE [ie. B(a)P x 10] (b)	
	32 // 228 (0.5 // 3)	8 // 57 (0.5 // 4)
a) Based on 444, 24 hour average samples taken at five sites in Windsor; the first value is the lowest mean B(a)P concentration and the second value is the highest 90th percentile concentration.		
b) 'Total Carcinogenic PAH' was estimated (see approach # 2 sect. 3.1.1) from concentrations of B(a)P (ie. by multiplying B(a)P concentrations by a factor of 10);		
c) Assuming the following weights and inhalation rates per day (ie. per 24 hour period): Adult: 70 kg; 20 m <sup>3</sup> /day Child: 15 kg; 5 m <sup>3</sup> /day		

### 3.1.2 Microenvironments

It is reasonable to assume that the daily PAH intakes associated with typical personal exposure patterns will be different from those based on fixed site monitoring data. With most of the substances on the Windsor focus list, this evaluation was based on various microenvironmental concentrations. For the purpose of scoping population exposures, the set of typical receptors in Table 3 below was normally considered. Examples of the receptor types and/or their characteristics are also included in Table 3. For PAHs, Windsor-specific microenvironment and personal exposure concentrations were not available. As a surrogate, indoor concentrations acquired in other studies were used to represent the range of 'typical personal exposure' patterns. The concentration from these studies and the associated estimated daily intakes (in ng/day) are summarized in Table 4.

Table 3. Receptors With Typical Personal Exposure Patterns

NAME OF RECEPTOR TYPE	CHARACTERISTICS	NAME OF RECEPTOR TYPE	CHARACTERISTICS
Average Office Worker (Non-smoking)	Eg. - Typical office worker (Based on Windsor volunteers and US EPA TEAM study; not smoking at home)	High Outdoor Receptor	Eg. - Construction workers; - Bicycle couriers - Police - Long distance runners
Average Office Worker (Smoker Environment)	Eg. - Typical office worker (Based on Windsor volunteers and US EPA TEAM study; smoking at home)	High Indoor Receptor	Eg. - 'Shut-ins'- Invalids - Elderly, non-mobile
Average Youth	Eg. Special exposures at shopping malls and athletic facilities (pools) in addition to school;	High Commuting Receptor	Eg.- Bus drivers - Taxi drivers - Delivery/ Distribution Services
Average Child (Non-Smoker Home & No Exposure to Tobacco Smoke)	Eg. Similar to average office worker except 'School' replaces 'Office';	Active Receptor # 1	Eg.- 7 hr/week in Bingo Hall or Bar
Average Child (Non-Smoker Home & Typical Exposure to Tobacco Smoke)	Eg. Includes typical times that children may be in proximity to tobacco smoke, outside the home, based on activity pattern studies;		
Average Child (Smoker Home with Exposure to Tobacco Smoke)	Eg. Child living in a house where there is a smoker		

**Table 4. Estimated Daily Intakes of B(a)P Associated With Indoor Air Environments (ie. surrogate data taken in indoor environments<sup>70</sup> to represent 'Typical personal exposures').**

Indoor Air Environment (a)	Concentration ng/m <sup>3</sup>	Adult (b) ng/day (ng/kg-day)	Child (b) ng/day (ng/kg-day)
Median (a)	0.8	16 (0.2)	4 (0.3)
Range of values (Minimum to Maximum values) (a)	0.1 - 8	2 - 160 (0.03 - 2.3)	0.5 - 40 (0.03 - 2.7)
<p>a Based on studies cited in Menzie et. al. Environ. Sci. Technol. 1992, 26, 1278-84. This paper lists 'carcinogenic PAH' concentrations which were developed by the authors from B(a)P data by multiplying by 10. The 'original' B(a)P values for this Table 4 were regenerated by dividing by 10.</p> <p>b Assuming the following weights and inhalation rates per day (ie. per 24 hour period):  Adult: 70 kg; 20 m<sup>3</sup>/day  Child: 15 kg; 5 m<sup>3</sup>/day</p>			

In order to place the above inhalation exposures (ie. intakes) in perspective, it is appropriate to compare to daily intakes that people who smoke may experience.

### 3.1.3 Smoking.

PAHs have been detected in cigarette smoke and exposure occurs both through direct inhalation by smokers and from side stream smoke.

There is information on specific PAHs and also on total and total carcinogenic PAHs. The average yield per cigarette of the two carcinogenic PAHs benzo[a]pyrene (B(a)P) and benz[a]anthracene (B(a)A) for mainstream smoke is 20-40 and 20-70 ng, respectively, for non-filter cigarettes (Ref. 71; t.3.2, p.53). For the Kentucky reference 1R4F filter cigarette, the yields are 9.2 and 10 ng (Ref 71; t.3.1, p.47). The yield for sidestream smoke for the reference filter cigarette is 0.1-0.15 and 0.2 ug/cigarette (Ref 71; t.3.1, p.47; t.3.5, p.56). The authors note that filters and changes in tobacco processing have reduced mainstream deliveries considerably whereas sidestream deliveries have remained fairly constant.

A person who smokes a pack a day (ie. 25 cigarettes) would therefore inhale between 250 and 1000 ng/d of B(a)P (ie. taking 40 ng/cigarette as the average yield of B(a)P). The lower bound would apply to filter cigarettes.

Several carcinogenic PAHs, including B(a)P and B(a)A have been identified in environmental tobacco smoke, especially in the particulate phase (Ref. 71; t.4.4 and 4.5, p.72 and 73). The sidestream smoke is, of course, greatly diluted by indoor air and it is difficult to demonstrate a definite contribution from smoking to indoor concentrations of PAHs. Appendix 7 of Guerin *et al.*<sup>71</sup> summarizes the results of many studies comparing indoor air with smokers present and controls, usually outdoor air. The data for B(a)P and B(a)A suggest that smoking does not elevate concentrations in indoor air by more than about a factor of two.

Menzie *et al.*<sup>70</sup> report that B(a)P makes up about 5% and 30% of PAHs in outdoor air and have selected



10% as a reasonable number (see s. 3.1.1). Therefore, the amount of carcinogenic PAHs can be estimated by multiplying the amount of B(a)P by 10. The authors<sup>70</sup> state that *mainstream smoke from unfiltered cigarettes may contain 0.1-0.25 ug/cigarette of carcinogenic PAHs*. The exposure of smokers to carcinogenic PAHs is then 2.5 to 6.25 ug/d. Butler *et al.*<sup>72</sup> quote an EPA study which estimates an average daily intake of 600 ng of B(a)P from smoking, based on an average 25 cigarettes per day. This translates to 6 ug/d of carcinogenic PAHs. A report prepared for MOEE (Ref. 73; t.7-2, p.7-23) states that the mid-range concentration of carcinogenic PAHs (undefined) is 0.14 ug/cigarette, which translates into a daily intake of 3.5 ug. These numbers are in agreement with the values calculated from the B(a)P exposures derived from the Guerin *et al.*<sup>71</sup> data or 2.5-10 ug/d (see above).

Non-smokers who are heavily exposed to environmental tobacco smoke inhale the equivalent of 1/3 to 3 cigarettes per day or 10 to 120 ng of B(a)P (Blot and Fraumeni<sup>74</sup>). Vainio<sup>75</sup> states that the exposure of non-smokers to environmental tobacco smoke would be about 1% of that of active smokers or 2.5 to 10 ng/day, whereas Remmer<sup>76</sup> (1987) gives as an upper limit the equivalent of only 1/5 of a cigarette per day or about 2 to 8 ng/day. Hiller<sup>77</sup>, quoting other authors, gives intakes ranging from a low of 0.001 cigarette equivalents (CE)/hr or 0.01 CE/day, assuming 12 hr exposure, to a high of 27 CE/day. The higher value is clearly anomalous as the range claimed by the other authors is 0.001 to 0.2 CE/hr. The lower value gives an intake of 0.1 to 0.4 ng/day. Since smoking does not appear to increase the concentration of B(a)P markedly, the lower end of the range is more likely; that is, somewhere around 5 ng/d. Butler *et al.*<sup>72</sup> state that a person exposed to environmental tobacco smoke inhaled = 40 ng/d of B(a)P in winter and 6 ng/d in summer. His intake was about twice that of his wife, who did not share his occupational exposure. The intake of carcinogenic PAHs is then in the range of 1 - 1200 ng/day, although the upper limit may well be an overestimate.

It is also important to place the inhalation exposures (ie. intakes) in Windsor into perspective, relative to general exposures from other media (ie. see s. 3.2).

### 3.2 Other Routes

In this section, possible non-inhalation routes of exposure (ie. ingestion and dermal) are assessed.

#### 3.2.1 Ingestion of Food

In the THEES study<sup>72</sup>, the concentrations of benzo[a]pyrene in indoor and outdoor air, food, water and soil in a total of 8-10 homes (14-15 persons) were monitored for two winter and one summer periods. Daily meal portions (ie. prepared food) of one member in each household were collected and composited into weekly samples before analysis for B(a)P. The concentrations were converted to ingested dose by multiplying with the average food ingestion rate. Total absorption was assumed.

This study<sup>72</sup> showed that the range of dietary B(a)P doses spanned three orders of magnitude and varied from week to week for the same individual. This variability is ascribed to *individual differences in food habits and cooking methods as well as the source of the foods*. The ingested doses in winter were less than half the doses in summer. According to the self-reported food diaries, this difference cannot be ascribed to seasonal differences in cooking style, such as barbecuing. Table IV<sup>72</sup> gives the following ingestion rates:

Winter period 1		
mean±stand.dev.		87±135 ng B(a)P/d
range		1-572
n		20



period 2		
mean±stand.dev.		94±134 ng B(a)P/d
range		6-575
n		20

<u>Summer</u>		
mean±stand.dev.		195±303 ng B(a)P/d
range		2-1149
n		18

The authors selected 140 ng B(a)P/d as the mean daily intake.

Menzie *et al.*<sup>70</sup>, using data from the US Dept. of Agriculture, determined an average diet for US males as well as a vegetarian and a heavy meat diet comprising products with high PAH levels. Potential low and high intakes of carcinogenic PAHs, for the three different types of diet, shown in Fig. 1 of the paper, are:

average diet:	1.2 and 4.8 ug carcinogenic PAH/day
vegetarian diet:	2.8 and 8.7
heavy meat:	6.1 and 11.6

The authors list the following eight PAHs that are typically considered as possible or probable carcinogens: benzo[a]anthracene, chrysene, benzo[b]fluoranthene, benzo[k]fluoranthene, benzo[a]pyrene, indeno[1,2,3-c,d]pyrene, dibenzo[a,h]anthracene, and benzo[g,h,i]perylene.

The authors assume that B(a)P makes up about 10% of total carcinogenic PAHs. The assumed B(a)P content in the average diet - 120-480 ng/d - is close to the mean daily intake - 140 ng/d - measured by Butler *et al.*<sup>72</sup>.

The major contributor to the 'average diet' is grains; for both 'vegetarian diets', vegetables; and for the 'high meat diet', meats and fish. Charcoal broiled or smoked meat and fish are major sources of carcinogenic PAHs. The levels in smoked or charcoal broiled meat and fish are 9 to 35 ng/g and about two orders of magnitude higher than in non-smoked or broiled meats and fish. Atmospheric deposition is considered as the primary pathway for PAH contamination of vegetables.

MOEE (Ref.73, t.7-2; p.7-23) reports an intake of carcinogenic PAHs (undefined) of 0.72 ug/d, which would translate into 72 ng B(a)P/d. This estimate is somewhat lower than the two above. The main sources are, in order, meats (including cured), chicken, baked goods and vegetables. The meats and chicken are assumed to be cooked.

In conclusion, the B(a)P intake from an average diet is of the order of 70-150 ng/d (assumed that a child's diet falls into this same range), with a high of 500 ng/d - and of carcinogenic PAHs, about 10 to 20 times as much. Intakes from vegetarian and high meat diets are 2-3 times higher.

### 3.2.2 Drinking water.

The Ministry survey of drinking water from Windsor in 1990 did not find any detectable levels of

carcinogenic and non-carcinogenic PAHs. The detection limits range from 5 to 50 ng/L. The study by Butler *et al.*<sup>72</sup> reports that all drinking water levels were below the detection limit of 0.1 ng/L. Menzie *et al.*<sup>70</sup> state the median concentration of carcinogenic PAHs is 2.8 ng/L, with a range of 0.1-62 ng/L. A report prepared for MOEE (Ref. 73, t.7-2, p.7-23) states that the median concentration of carcinogenic PAHs is 2.1 ng/L, based on US data.

It is clear that the intake from drinking water is quite small. For an ingestion of 2L of drinking water, the intake is probably < 5 ng/d.

### 3.2.3 Soil

PAHs were sampled by the MOEE<sup>78</sup> in 1990 at 12 urban stations located primarily in municipal parks in Windsor or neighbouring urban municipalities and 5 rural stations located on the lawns of rural, residential properties in Essex County about 15 km from the Detroit River. The locations had a maintained sod grass cover. Six cores of the top 5 cm of the soil were taken at each station for the analysis of organics and stored frozen until analysis. The concentrations are reported as ng/g dry weight.

For the eight carcinogenic PAHs (see Menzie *et al.*<sup>70</sup> and s. 3.2.1 for listing of these PAHs), only a third of the 17 stations reported concentrations that are not qualified by either <T or <W (Ref. 78, t.4). The former means that the substance has been detected but that little significance should be attributed to a single determination, since it may well be a false positive. The latter means that, in effect, it is below the detection limit. The stations can be divided into three groups: those, where the measured concentrations of 7 or 8 of the eight carcinogenic PAHs are not qualified by <T or <W; those, where 1 to 3 PAHs are not qualified and the others. Only three urban stations close to the Detroit River in the vicinity of the Ambassador Bridge and the Detroit Tunnel and one rural station fall into the first group. The rural station (C3) has concentrations that exceed any of the urban locations, possibly as the result of some isolated activity there. Four urban stations fall into the second group; the remaining stations fall into the third. On the basis of these data, it is apparent that the concentrations of PAHs in the soil shows a decrease with increasing distance in a southeasterly direction away from the Detroit River.

The median and average soil concentrations (ng/g) in Windsor, using all values including < T and < W, are:

		<u>Median</u>	<u>Average</u> <sup>1</sup>	<u>Maximum</u>
benzo[a]pyrene	- urban	65	128±136	453
	- rural <sup>2</sup>	<20	-	910
sum of all eight carcinogenic PAHs	- urban	1310	1470±1200	3470
	- rural	<220	<220	7320 <sup>3</sup>

- Notes:
1. Average ± standard deviation.
  2. Station C3 with highest concentration omitted. See discussion above.

3. For station C3. This represents also the maximum concentration for all of the stations, both urban and rural.

It should be noted that the ratio (average carcinogenic PAHs/average B(a)P) for the urban stations is 11.5.

A reasonable estimate for the amount of ingested soil and dust is 80 mg/d for children and 20 mg/d for adults (Ref. 79, Appendix 1), although values as low as 0 for children <1 y, 40 mg/d for children 1-6 y and 10 mg/d for persons > 6 y have been used (Sheehan *et al.*<sup>80</sup>). Using the MOEE soil ingestion values, the average intakes of B(a)P and total carcinogenic PAHs from urban soil in Windsor are:

B(a)P:	
adults:	2.6 ng/d
children:	10
carcinogenic PAHs:	
adults:	30 ng/d
children:	120

Based on a soil intake of 50 mg/d, Menzie *et al.*<sup>70</sup> estimate a potential dose of carcinogenic PAHs from 3 to 300 ng/d, with a median value of 60, although they also point out that the potential dose could be higher if some of the soil that is ingested is road dust tracked into homes. Butler *et al.*<sup>72</sup>, as part of the THEES study, report B(a)P concentrations in soil from 51-467 ng/g, which are *comparable to reported background levels*. Furthermore, Butler *et al.*<sup>72</sup> note that, assuming a B(a)P concentration of 500 ng/g, an EPA soil ingestion model yields an "upper end of average" intake range of 7-36 ng/day for soil ingestion exposure, depending on the age of the individual and duration of exposure.

ATSDR (Ref. 81, t.5-5, p.143) reports the following ranges for B(a)P:

rural soil:	2-1300 ng B(a)P/g
agricultural soil:	4.6-900
urban soil:	165-220

The levels found in the soil in Windsor are in the same range as found elsewhere. Similarly, the ingestion of B(a)P and carcinogenic PAHs are in the same range as found elsewhere.

### 3.2.4 Dermal

#### 3.2.4.1 During Showering and Bathing

The available data on PAHs in drinking water suggest that the concentrations are most likely <10 ng/L and probably <1 ng/L (see s. 3.2.2). A high efficiency of degradation of PAHs from chlorination has been

reported (Ref. 81, p. 138) The dermal absorption during showering and bathing would therefore be expected to be very small, especially since the PAHs partition preferentially to suspended particles in the water (Ref. 81, p. 134).

### 3.2.4.2 Contact With Soil and Dirt

The experimental data for the dermal absorption of B(a)P from soil, both *in vivo* and *in vitro*, has been reviewed in an EPA report (Ref. 82, p. 6-22 *et seq.*). Because of the wide range of the fraction of the applied dose that is absorbed, the report does not recommend any particular values.

The *in vitro* experiments with rat skin by Yang *et al.* (cited in the EPA report<sup>82</sup>) using soil contaminated with crude petroleum and a B(a)P concentration of  $\approx 100$  ppm indicated that between 1.3% (56 mg soil/cm<sup>2</sup>) and 8.4% (9 mg soil/cm<sup>2</sup>) of the initial applied dose of B(a)P was absorbed in 96 hr. Another experiment in which radioactive B(a)P was applied to the back of rats showed that, after 96 hr, the cumulative dose in excreta and tissues was 9.6%.

The *in vitro* experiments with human skin by Wester *et al.* (cited in the EPA report<sup>82</sup>) showed that after 24 hr, when the surface of the skin was washed with soap and water, on an average 1.4% of the applied dose (10 ppm in soil) was found in the skin and only 0.01% in the plasma receptor fluid. The surface loading was 40 mg soil/cm<sup>2</sup>. The B(a)P in the skin can be expected to migrate over a period of time into the plasma. *In vivo* experiments with rhesus monkeys showed that 13.2% of the topically applied dose was absorbed on the average over 24 hr.

The most appropriate daily loading of soil on exposed skin is estimated to be 1.8 mg/cm<sup>2</sup> (range 0.5 - 2.8 mg/cm<sup>2</sup>). The exposed area is taken to be 1580 cm<sup>2</sup> for a child and 1980 cm<sup>2</sup> for an adult, or basically the hands and arms (Sheehan, P.J. *et al.*<sup>80</sup>).

Taking the amount absorbed as 1.4 - 13% of the same dose on the skin and using the average soil concentration of 128 ng/g or a loading of 0.23 ng/cm<sup>2</sup> (s.3.2.3), the amount of B(a)P absorbed through the skin in 24 hr is:

adults:	6.4-59 ng B(a)P/d
children:	5.1-47 ng B(a)P/day

It is unlikely that the skin is as contaminated in winter as in summer or that the hands and arms are covered by dust 24 hours a day. Therefore, the amount absorbed daily when averaged over the period of a year would be less than the rates calculated above.

Butler *et al.*<sup>72</sup>, Menzie *et al.*<sup>70</sup> or MOEE<sup>73</sup> do not give any estimates of the amount of B(a)P absorbed through the skin, although Butler *et al.*<sup>72</sup> state, quoting EPA, that dermal absorption is *an exposure route of relatively little significance*. This and the experimental results suggest that the dermal absorption is more likely to be closer to the lower than the upper end of the range calculated above.

### 3.2.4.3 From PAH Vapour in the Air

Since PAHs in air generally occur adsorbed on particulates, the amount present in vapour form is very



small. Therefore, the intake from air is expected to be insignificant.

#### 4.0 RISK CHARACTERIZATION AND PERSPECTIVES

Exposures, expressed as daily intakes in units of ng/day, were assessed in section 3. Inhalation, ingestion and dermal routes of exposure were considered. Table 5A and Table 5B below summarizes the daily intakes (or ranges of daily intakes) of B(a)P & B(a)P equivalents and, of 'carcinogenic PAHs' respectively, for adults and children, estimated in section 3. It should be noted that in section 3, the intakes for inhalation and sometimes for ingestion assumed 100% bioavailability. The intake for dermal exposures are amounts absorbed systemically and hence already include bioavailability considerations. Both Table 5A and 5B has two columns for both adults and children. The first set of columns (ie. '100 % Bioav') give the intakes with 100 % bioavailability having been assumed; the second set (ie. 'Bioav. Incl.'), gives intakes for which bioavailability has been taken into consideration (ie. if information was available as noted in the footnotes). This second set of columns should give a better picture of the relative importance of various exposure routes. As far as comparison to exposure guidelines and intakes associated with cancer risk, the intakes in the first set of columns of Table 5A and 5B will be used since the exposure guidelines are also expressed as intakes for which we have assumed 100 % bioavailability.

To characterize risks, the various exposure guidelines discussed in Section 2 are compared to the estimated exposures from inhalation and other routes as discussed in Section 3. Because of the assumptions, uncertainties and ranges of values available from both exposures (see Table 5A and 5B) and the various exposure guidelines (see Table 1), risk characterization is most appropriately done by comparison of ranges of values.

Table 6 below provides a graphic representation of this comparison of exposures, exposure guidelines and intakes associated with inhalation cancer risk, based on ng intake/day (ie. 'INTAKE in Nanograms per day' increasing upwards on the vertical scale).

The middle section of Table 6, "Exposures", depicts the exposures calculated in Section 3, expressed as intake/day (ie. ng/day). The exposures depicted are: *Outdoor Air Quality* - the exposure from spending 100 % of the day outdoors; *Typical Outdoor Exposure* - the exposure from three hours only outdoors, provided for perspective on the contribution to risk solely from contaminants present in outdoor air; *Typical Personal Exposures* - the range of exposures associated with 'personal activity patterns' (ie. for PAHs, surrogate indoor air values were used because of the lack of Windsor specific data) combining periods of indoor, outdoor and various microenvironment exposures. Exposure scenarios are included for adults and children, assuming 20 and 5 m<sup>3</sup>/day inhalation rates respectively. For 'outdoor air quality' (ie. 100% outdoor exposure), for 'typical outdoor exposures' (ie. 3 hr), and for the 'typical activity patterns' the ranges shown, bracket the lowest mean to the highest 90th percentile.

For 'outdoor air quality' and for 'typical outdoor exposures' (ie. 3hr) two sets of ranges are shown side by side. The first bar in each set is for B(a)P only. The second bar in each set (ie. labelled on the bottom of the bars with "E") is for B(a)P equivalents. In both sets (ie. all 4 bars), the ranges shown bracket the lowest mean and the highest 90th percentile. For 'personal activity patterns', which are represented by surrogate indoor air values, the range indicates the overall range of possible exposures (s. 3.1.2 and Table 4).

Above some of the bars is a horizontal line labelled "C" PAH. These represent likely upper bounds for 'carcinogenic' PAHs obtained either by multiplying the B(a)P concentrations by 10 or using the total



carcinogenic PAH from the available data (ie. see s. 3.1.1 - outdoor air; s. 3.1.2 - typical personal exposures; s. 3.1.3 - smoker; and see Table 5A and 5B below). These are shown primarily for appreciating the range of risks calculated later in Table 7.

For perspective purposes, the exposures of smokers, directly from smoking activity is also depicted in the exposure section of Table 6.

The left section of Table 6, "Exposure Guidelines", expresses the various guidelines discussed in Section 2 in terms of calculated "allowable" intake/day for adults and children. The values are taken from Table 1. Within each type of guideline group (eg. outdoor air) ranges of exposure guidelines, when available, are indicated. Thus, ranges of Air Quality Guidelines (ie. 'Outdoor Air') and Occupational guidelines (ie. 'Workplace Air') are shown. The horizontal line across the 'Outdoor air' bar represents the Ontario guideline. Comparison of "Exposure Guidelines" to "Exposures" should be done with care. For example, occupational guidelines are included for perspective purposes only. For caveats regarding this comparison see section 4.1.1 of the main report.

The right section of Table 6, "Intakes Associated With Cancer Risk", shows the intakes associated with different levels of cancer risk. Ranges of carcinogenic risk levels (associated with  $1 \times 10^{-5}$  risk and  $1 \times 10^{-6}$  risk) are depicted. Comparison of "Exposures" to "Intakes Associated With Cancer Risk" is appropriate for adult exposures only, since cancer risk estimates apply to a lifetime of exposure and people are adults for the majority of their lives. Adult exposures in the bars of the "Exposure" section fall in the top 70 % of the bars which represent exposures of adults and children.

Based on the tabular analysis (Table 5A and 5B) and the graphic risk characterization (Table 6), the following observations and deductions can be made:

*Because of the many sources of non-uniform data for PAHs and B(a)P, it was necessary to provide intakes in terms of B(a)P itself, as B(a)P equivalents, and as 'carcinogenic PAHs' (ie. generally this is 10 x the B(a)P levels; in some cases it is based directly on the available data). Note that in Table 5A and 5B, these different intake values are identified as B(a)P, as "E" values and as "C" values respectively. Also, as implied by Table 1, in section 2, almost all guidelines available for assessing PAHs are given in terms of B(a)P.*

#### Health messages:

1) Considering the B(a)P and B(a)P equivalent intakes (ie. 'Bioav. Incl.' column in Table 5A) and, the 'carcinogenic PAH' intakes (ie. 'Bioav. Incl.' column in Table 5B) ingestion is the primary route of exposure. Furthermore, the food intake entry of 'carcinogenic PAHs' in Table 5B is for average diets and for heavy meat diets (ie. see footnote 'd' in Table 5B) the ingestion exposure route would be even more dominant. Thus, the overall picture indicates that ingestion is the primary route of exposure for both B(a)P and PAHs and can be much greater than other routes when heavy meat diets are involved. Inhalation appears to be the next most important route and is similar to dermal exposure.

2) Since no chronic acceptable exposure levels are available, no conclusions, regarding possible non-cancer chronic effects can be deduced.

3) The exposure that a smoker experiences exceeds both indoor and outdoor environments.

4) The most conservative range of available exposure guidelines are depicted in Table 6 under Intakes Associated with Cancer Risk. These guidelines were proposed by CDHS, the NJDEP, and the NYSDOH.

Table 5A. Summary of Estimated Daily Intakes and/or Range of Intakes (in ng /day), from Various Exposure Pathways (ie. intakes, assuming 100 % bioavailability and intakes with bioavailability taken into consideration) for B(a)P and B(a)P Toxic Equivalents (designated as "E" values).

EXPOSURE PATHWAY		ADULT ng/day (100 % Bioav.)	ADULT ng/day (Bioav. Incl.)	CHILD ng/day (100 % Bioav.)	CHILD ng/day (Bioav. Incl.)
INHALATION	Outdoor Air Quality - Windsor (ie. 100 % outdoor exposure)(a)	3.2 - 22.8 "E" 14 - 74	1 - 6.8 "E" 4 - 22 (f)	0.8 - 5.7 "E" 3 - 19	0.2 - 1.7 "E" 1 - 5.7 (f)
	Typical outdoor exposure (ie. = 3hr)(b)	0.4 - 2.9 "E" 1.8 - 9.3	0.1 - 0.9 "E" 0.5 - 2.8 (f)	0.1 - 0.7 "E" 0.4 - 2.4	0.03 - 0.2 "E" 0.1 - 0.7 (f)
	Typical personal exposures(ie. Table 4) (c)	2 - 160	0.6 - 50 (f)	0.5 - 40	0.2 - 12 (f)
	Smoking (e)	250 -1000	75 - 300 (f)		
INGESTION (i)	Food (d)	140	70	140	70
	Drinking water (g)	< 5	< 2.5	< 5	< 2.5
	Soil	2.5	1.3	10	5
	TOTAL (Ingestion)	148	74	155	78
DERMAL	During showering (h)	-	-	-	-
	Contact with soil & dirt		6.5 - 60		5 - 47
	TOTAL (Dermal)		6.5 - 60		5 - 47
<p>"E" values - Calculated from the measured PAHs using TEFs as described in section 3.1.1, approach (1);</p> <p>a.) Range of intakes is associated with the range of the 'mean' to '90th percentile' concentrations in outdoor air. It is to be noted that people are not exposed 24 hours to outdoor air. This estimation assumes 100 % exposure to outdoor air and is a measure of outdoor air quality per se and not of actual exposure.</p> <p>b.) Range of intakes calculated from the 'mean' to '90th percentile' concentrations in outdoor air and assuming a 'typical' outdoor air exposure of = 3 hr(ie. corresponding to breathing 2.5 m<sup>3</sup>/3hr for adults and 0.63 m<sup>3</sup>/3hr for children.</p> <p>c.) Range of intakes is estimated from the range of the 'minimum' and the highest maximum' concentrations based on several studies.</p> <p>d.) See s. 3.2.1. The value for B(a)P is the mean daily intake</p> <p>e.) The intake shown is the direct intake (ie. from average to upper bound estimate) of an adult smoker from smoking activity (ie. 'smoking') only (see s.3.1.3). Various smoking environments for adults and children have already been included in the 'typical personal exposure' scenarios.</p> <p>f.) An absorption rate of 30% was selected based on Willes et. al.<sup>2</sup> This includes absorption of PAHs deposited in the lungs plus material that is inhaled, cleared from the respiratory system by mucociliary clearance and swallowed.</p> <p>g.) See s. 3.2.2. The measured concentrations at Windsor were all &lt; detection limit. Other information from the available literature suggests that the intake is &lt; 5 ng/d of PAHs.</p> <p>h.) See s. 3.2.4.1.</p> <p>i.) An absorption rate of = 50% was selected for all ingestion routes (P. Muller, MOEE; personal communication. It is likely that absorption from soil is &lt; 50%.</p>					

Table 5B. Summary of Estimated Daily Intakes and/or Range of Intakes (in ng /day), from Various Exposure Pathways (ie. intakes, assuming 100 % bioavailability and intakes with bioavailability taken into consideration) for 'Carcinogenic PAH's (designated as "C" values)

EXPOSURE PATHWAY		ADULT ng/day  (100 % Bioav.)	ADULT ng/day  (Bioav. Incl.)	CHILD ng/day  (100 % Bioav.)	CHILD ng/day  (Bioav. Incl.)
INHALATION	Outdoor Air Quality - Windsor (ie. 100 % outdoor exposure)(a)	"C" 32 - 228	10 - 68 (f)	"C" 8 - 57	2.5 - 17 (f)
	Typical outdoor exposure (ie. = 3hr)(b)	"C" 4 - 28.5	1 - 8.6 (f)	"C" 1 - 1.2	0.3 - 2.1 (f)
	Typical personal exposures(ie. Table 4) (c)	"C" 20 - 1600	6 - 480 (f)	"C" 5 - 400	1.5 - 120 (f)
	Smoking (e)	"C" 2500 - 10,000	750 - 3000 (f)		
INGESTION (j)	Food (d)	"C" 1200 - 4800	600 - 2400	"C" 1200 - 4800	600 - 2400
	Drinking water (g)	< 5	< 2.5	< 5	< 2.5
	Soil (h)	"C" 30	15	"C" 120	60
	TOTAL (Ingestion)				
DERMAL	During showering (i)				
	Contact with soil & dirt (k)				
	TOTAL (Dermal)				

"C" values - Calculated from B(a)P concentrations by multiplying these by 10 (ie. as described in section 3.1.1 approach # (2) and also in the 'smoker', 'ingestion' and 'dermal' sections).

a.) Range of intakes is associated with the range of the 'mean' to '90th percentile' concentrations in outdoor air. It is to be noted that people are not exposed 24 hours to outdoor air. This estimation assumes 100 % exposure to outdoor air and is a measure of outdoor air quality per se and not of actual exposure.

b.) Range of intakes calculated from the 'mean' to '90th percentile' concentrations in outdoor air and assuming a 'typical' outdoor air exposure of = 3 hr(ie. corresponding to breathing 2.5 m<sup>3</sup>/3hr for adults and 0.63 m<sup>3</sup>/3hr for children.

c.) Range of intakes is estimated from the 'minimum' and the highest 'maximum' concentrations based on several studies.

d.) The intake for total PAHs is for the average diet. A heavy meat diet may result in an intake of 11,600 ng/d.

e.) The intake shown is the direct intake (ie. from average to upper bound estimate) of an adult smoker from smoking activity (ie. 'smoking') only (see s. 3.1.3). Various smoking environments for adults and children have already been included in the 'typical personal exposure' scenarios.

f.) An absorption rate of 30% was selected based on Willes et. al.<sup>2</sup> This includes absorption of PAHs deposited in the lungs plus material that is inhaled, cleared from the respiratory system by mucociliary clearance and swallowed.

g.) See s. 3.2.2. The measured concentrations at Windsor were all < detection limit. Other information from the available literature suggests that the intake is < 5 ng/d of PAHs

h.) See s. 3.2.3. The carcinogenic PAHs included are the same as for food ingestion

i.) See s. 3.2.4.1.

j.) An absorption rate of = 50% was selected for all ingestion routes (P. Muller, MOEE; personal communication). it is likely that absorption from soil is < 50%.

k.) See s. 3.2.4.2. There is no dermal absorption data for PAHs other than B(a)P.





As shown in Table 6, they overlap with the estimated exposures associated with 'outdoor air quality' when these exposure estimates are based on B(a)P only (ie. unlabelled 1st bar under Exposures) or on B(a)P equivalents (ie. 2nd bar, labelled "E" under Exposures). When exposure estimates are based on 'carcinogenic PAHs' (ie. B(a)P concentrations multiplied by 10, as described in section 3.1.1), they still overlap with the risk based guidelines shown on the right side of Table 6. Because people are adults for the majority of their lives, these intakes associated with cancer risk are depicted for adults only.

The inhalation intakes for adults associated with 'outdoor air quality' (ie. 100 % outdoor exposure), 'typical outdoor exposure' (ie. 3 hr) and 'typical personal exposures' (in this case based on surrogate indoor air data since Windsor specific data was not available), expressed in various ways (ie. as B(a)P, 'carcinogenic PAHs') are summarized in Table 7. Using the various methods, defined in Table 7, and the various potencies from the three agencies, the range of risks associated with 'outdoor air quality' (ie. 100% outdoor exposure) is between  $3.6 \times 10^{-7}$  and  $2.0 \times 10^{-5}$ . Similarly the range of risks associated with 'typical outdoor exposures' (ie. 3 hr) is between  $4.7 \times 10^{-8}$  and  $2.5 \times 10^{-6}$ . Similarly the range of risks associated with 'typical personal exposures' is between  $5.2 \times 10^{-7}$  and  $1.4 \times 10^{-4}$ .

The risks associated with 'typical personal exposures' (ie. indoor values) are slightly higher than the risks associated with 'outdoor air quality' which in turn is higher than 'typical outdoor exposures'. In this case, the risk estimate for 'typical personal exposures', based on surrogate indoor values, is based on 100 % indoor exposure and is therefore a worst case estimate.

This range of risk analysis is summarized in Table 7. It should be further noted, that this risk characterization (ie. using carcinogenic risk based limits) is based on an assumed lifetime exposure (i.e., 24 hours, every day, for 70 years) and hence is a very conservative assumption.

5) The exposure that a smoker experiences is considerably higher than any of the exposures associated with 'personal activity patterns', 'outdoor air quality' and 'typical outdoor exposures'.

6) Considering the information in Table 5A and 5B the exposures from the *non-inhalation* pathways are:

- *Ingestion* of food, water and soil:

B(a)P: 148 ng/day (= 74 ng/day absorbed)

'Carcinogenic PAH': 1200 - 4800 ng/day (= 600 -2400 ng/day absorbed)

- up to 11600 ng/day (= 5800 ng/day absorbed) for a heavy meat diet

- *Dermal* absorption (values indicated all absorbed):

adult: 6.5 - 60 ng/day;

child: 5 - 47 ng/day;

The intakes associated with ingestion and dermal exposure are approximately 4 - 16 fold above the available ingestion guidelines (ie. 15 - 300 ng/day in Table 1)

9) These intakes (ie. ingestion and dermal) also overlap with intakes associated with cancer risk from oral exposures (ie. not shown in Table 6 but see Table 1 - 'Allowable' intakes, associated with oral cancer potency factor under Ingestion Guidelines). For average diets, ingestion and dermal exposures are slightly above a risk of  $1 \times 10^{-5}$ . For heavy meat diets, the risks can be as high as  $1 \times 10^{-3}$ .



**Table 7. Range of Inhalation Cancer Risks Associated with Estimated Intakes(ie. for adult exposures only) of PAHs**

RANGE of INHALATION INTAKES				POTENCY (a)		RANGE of RISKS
Environment	Method (b)	Unit ng/day	Unit mg/kg/day	Agency	Unit (mg/kg-d) <sup>1</sup>	
OUTDOOR AIR QUALITY (Windsor)	# 1 (c)	14 - 74	2 x 10 <sup>-7</sup> - 1.1 x 10 <sup>-6</sup>	CDHS NJDEP	6.1	1.2 x 10 <sup>-6</sup> - 6.7 x 10 <sup>-6</sup>
				NYSDOH	1.8	3.6 x 10 <sup>-7</sup> - 2.0 x 10 <sup>-6</sup>
OUTDOOR AIR QUALITY (Windsor)	# 2 (d)	32 - 228	4.6 x 10 <sup>-7</sup> - 3.3 x 10 <sup>-6</sup>	CDHS NJDEP	6.1	2.8 x 10 <sup>-6</sup> - 2.0 x 10 <sup>-5</sup>
				NYSDOH	1.8	8.3 x 10 <sup>-7</sup> - 5.9 x 10 <sup>-6</sup>
				OVERALL RANGE OF RISKS(Method #1 & 2): 3.6 x 10 <sup>-7</sup> - 2.0 x 10 <sup>-5</sup>		
TYPICAL OUTDOOR EXPOSURE (ie. = 3 hr.)	# 1 (c)	1.8 - 9.3	2.6 x 10 <sup>-8</sup> - 1.3 x 10 <sup>-7</sup>	CDHS NJDEP	6.1	1.6 x 10 <sup>-7</sup> - 7.9 x 10 <sup>-7</sup>
				NYSDOH	1.8	4.7 x 10 <sup>-8</sup> - 2.3 x 10 <sup>-7</sup>
TYPICAL OUTDOOR EXPOSURE (ie.= 3 hr.)	# 2 (d)	4 - 28.5	5.7 x 10 <sup>-8</sup> - 4.1 x 10 <sup>-7</sup>	CDHS NJDEP	6.1	3.5 x 10 <sup>-7</sup> - 2.5 x 10 <sup>-6</sup>
				NYSDOH	1.8	1.0 x 10 <sup>-7</sup> - 7.4 x 10 <sup>-7</sup>
				OVERALL RANGE OF RISKS(Method # 1 & 2): 4.7 x 10 <sup>-8</sup> - 2.5 x 10 <sup>-6</sup>		
TYPICAL PERSONAL EXPOSURES (ie. based on surrogate indoor data)	# 2 (e)	20 - 1600	2.9 x 10 <sup>-7</sup> - 22.9 x 10 <sup>-6</sup>	CDHS NJDEP	6.1	1.8 x 10 <sup>-6</sup> - 1.4 x 10 <sup>-4</sup>
				NYSDOH	1.8	5.2 x 10 <sup>-7</sup> - 4.1 x 10 <sup>-5</sup>
				OVERALL RANGE OF RISKS: 5.2 x 10 <sup>-7</sup> - 1.4 x 10 <sup>-4</sup>		
a. These are equivalent potency factors calculated from the unit risks proposed by the agencies listed; assumed adult weight of 70 kg and 20 m <sup>3</sup> per day.						
b. This columns gives the # of the method used and the B(a)P or PAH data used to develop the estimates; the individual methods are explained further in the other footnotes;						
c. Method # 1; this is B(a)P TEF approach, described in section 3.1.1, approach "(1)" and intake data is taken from Table 2.a;						
d. Method # 2; this is the 'total carcinogenic PAH' method( ie. B(a)P concentrations multiplied by 10); the method is described in section 3.1.1, approach "(2)" and intake data is based on the 'Carcinogenic PAH' section of Table 2.b.						
e. Method # 2; this is the 'total carcinogenic PAH' method(ie. B(a)P concentrations multiplied by 10, analogous to method in footnote 'd' above); data for typical personal exposure intakes(based on surrogate indoor data), is taken from Table 4, with B(a)P concentrations having been multiplied by 10;						

**Regulatory compliance messages:**

10) The risk characterization in Table 6 indicates that, for the inhalation receptor exposures considered:

- The exposures potentially associated with outdoor air quality, for adults, youth and children, overlap with and exceed the air quality guidelines of various jurisdictions. These exposures exceed the Ontario guideline.

- Exposures associated with typical outdoor exposure (ie.3 hr) fall below the air quality guidelines of various jurisdictions (ie. using the highest B(a)P equivalent value).

- Exposures associated with personal activity patterns, represented by surrogate indoor air values, overlap with and exceed the air quality guidelines of various jurisdictions.

It should be noted that these air quality guidelines may be of different types. Some are purely health based and some are regulatory and therefore may have been influenced by various risk management considerations. The regulatory guidelines may also have different uses (eg. judging the acceptability of air quality per se or judging the incremental addition by a source to the existing air quality).

11) Table 6 also indicates that all the inhalation exposures are less than the range of occupational levels.

12) MOEE is presently reviewing PAHs for the purposes of standard setting and is also reviewing the basis of the existing standard for B(a)P.

#### Summary and recommendations:

- ♦ Since no chronic acceptable exposure levels are available, no conclusions, regarding possible non-cancer chronic effects can be deduced.

- ♦ The range of estimated inhalation risks associated with 'outdoor air quality' (ie. 100% outdoor exposure) is between  $3.6 \times 10^{-7}$  and  $2.0 \times 10^{-5}$ . Similarly the range of risks associated with 'typical personal exposures' is between  $5.2 \times 10^{-7}$  and  $1.4 \times 10^{-4}$ . Since these levels of risk exceed  $1 \times 10^{-5}$ , a level generally deemed to be negligible, it is recommended that PAHs be considered as candidates for reduction of exposure.

- ♦ Exposures and therefore risks associated with 'typical personal exposures' (ie. indoor values) are slightly higher than the risks associated with 'outdoor air quality'. In this case, the risk estimate for 'typical personal exposures', based on surrogate indoor values, is based on 100 % indoor exposure and is therefore a worst case estimate.

- ♦ The exposure that a smoker experiences is considerably higher than any of the exposures associated with 'personal activity patterns' and 'outdoor air quality'.

- ♦ Ingestion is the primary route of exposure for both B(a)P and PAHs and can be much greater than other routes when heavy meat diets are involved.

- ♦ The intakes associated with ingestion and dermal exposure are approximately 4 to 16-fold above the available ingestion guidelines.

- ♦ Ingestion and dermal intakes overlap with intakes associated with cancer risk from oral exposures. For average diets, ingestion and dermal exposures are slightly above a risk of  $1 \times 10^{-5}$ . For heavy meat diets, the risks can be as high as  $1 \times 10^{-3}$ .

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## **APPENDIX 9**

### **RISK ANALYSIS FOR DIOXINS/FURANS**



APPENDIX 9  
RISK ANALYSIS FOR DIOXINS/FURANS

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## DIOXINS/FURANS

### DESCRIPTION and SOURCES of DIOXINS and FURANS.

The sources, fate, and environmental levels and physical, chemical and toxicological properties of dioxins and furans has been extensively reviewed<sup>1-16</sup>. Similar in chemical structure and biological properties, polychlorinated dibenzo-p-dioxins (or, simply "dioxins") and polychlorinated dibenzofurans (or, "furans") are two large families of chlorinated tricyclic aromatic compounds usually found together in the environment as complex mixtures. The toxicity of each compound depends on the number and position of the chlorine atoms within the molecules. Of the 75 possible dioxin isomers and 135 possible furan isomers, only the 17 which are chlorine substituted in the 2,3,7,8 positions are considered to pose a major health risk. 2,3,7,8-Tetrachlorodibenzo-p-dioxin (TCDD) has 4 chlorine atoms attached in the 2,3,7 and 8 positions and is the most toxic member of the dioxin family.

Dioxins and furans are not manufactured for any purpose. They are instead unwanted byproducts of a number of manufacturing and incineration processes, including: chlorine bleaching of pulp and paper; manufacture of phenoxy herbicides and pentachlorophenol wood preservative; incineration of municipal, biological and industrial wastes; wood combustion; gasoline combustion in motor vehicles; and various others. Their persistence in the environment has made them widespread throughout the various environmental media.

While human dioxin exposure is mostly from food, breathing urban air is also an important contributor to overall exposure levels. Drinking water and contact with contaminated soils or consumer products provide far less exposure to dioxins and furans when compared to exposure from food sources.

### 1. HAZARD IDENTIFICATION

The toxic and biological effects resulting from exposure to TCDD observed in several animal species include body weight loss, hepatotoxicity, porphyria, dermal toxicity, gastric lesions, thymus atrophy and immunotoxicity, reproductive effects and carcinogenicity<sup>1,6</sup>. Chloracne and related dermal lesions are the most frequent signs of TCDD toxicity in man.

TCDD is classified as a B2 carcinogen (probable human carcinogen) by the U.S. EPA and the International Agency for Research in Cancer (IARC). The federal government under the Canadian Environmental Protection Act (CEPA) recognizes its extreme toxicity to mammals and its ability to cause cancer in animals (Canadian Gazette, vol 124, No. 11, March 17, 1990; EC/HWC, 1990).

#### 1.1 Absorption and Metabolism

Due to the widespread occurrence of trace levels of dioxins and furans in the environment, their bioavailability from various environmental media is of importance. Animal studies indicate that ingestion of TCDD in the diet or vegetable oils can result in up to 80 % absorption. The amount of TCDD absorbed from ingested soil or flyash can be much lower (< 10 %), however, depending on the soil matrix.

Recent animal studies show that close to 100 % of TCDD is bioavailable from inhaled particulates. The absorption of chemicals on particles deposited in the lungs depends on factors such as the physical and chemical properties of the particles (size, solubility), the activity of alveolar macrophages and the reaction of the particles with the respiratory mucosa. The absorption has been studied in both animals and man (9, p.55; 26, p.49).

Particles and droplets greater than about 5  $\mu\text{m}$  do not penetrate into the alveoli of the lungs but are deposited in the nasal passages, trachea and bronchi and are cleared by ciliary action and swallowed. Smaller particles, especially those  $<2 \mu\text{m}$  do penetrate to the lungs and are deposited there. The amount deposited is about 30%. Recent animal studies show that close to 100% of the TCDD on the particulates that have been deposited is bioavailable. The remainder is swallowed. Of the amount swallowed, perhaps  $<10\%$  is absorbed (see above). Therefore, about 37% of the inhaled TCDD is bioavailable ( $30\% + 0.1 \times 70\%$ ).

Application of TCDD in solvents directly to the skin can result in 30% to 60% absorption of the amount applied. However, the dermal bioavailability of TCDD in soils, flyash, consumer products, or other contaminated media is orders of magnitude lower.

When mixtures of dioxins and furans are ingested, inhaled or absorbed through the skin, those compounds with chlorine atoms substituted in the 2, 3, 7 and 8 positions tend to be retained in body tissues. Distribution studies involving TCDD and 2,3,7,8-TCDF have indicated that the liver and adipose tissues are the major sites of storage for these compounds. In rodents, TCDD and TCDF will be found preferentially in the liver; in humans and monkeys, the majority of TCDD and TCDF is found in body fat. In humans, these 2,3,7,8-substituted dioxins and furans tend to accumulate in body fat and fatty organs such as the liver. Metabolism and excretion of these absorbed compounds is a relatively slow process in humans with half-lives of several years. Single dose half lives have been found to range from weeks to months in test animals. Excretion occurs mainly through the feces.

## 1.2 Toxicology

Exposure to acutely toxic doses of dioxins and furans may lead to a series of common biological and toxicological responses in mammals at the cellular, tissue, organ and organism levels. Lethal doses of TCDD in mammals range from 0.6  $\mu\text{g}/\text{kg}$  in male guinea pigs to 5051  $\mu\text{g}/\text{kg}$  in hamsters. Sublethal responses can include: wasting syndrome, which is characterized by progressive weight loss, decreasing food consumption and increasing weakness in test animals; various skin disorders, such as chloracne, alopecia, edema, hyperkeratosis and others; thymic atrophy, lymphoid involution and atrophy, and immune system effects; impaired liver function; altered hematological functions; endocrine and reproductive disorders; modulation of chemical carcinogenesis; induction of various enzyme systems. However, TCDD does not react with or damage the genetic material or chromosomes in these tests. The effects caused by exposure to TCDD cover a wide range and are species and sex dependent. Immature or developing animals are more sensitive to TCDD exposure than mature adults.

Even at low doses, TCDD can cause a number of serious health problems in test animals. The most sensitive toxic endpoints (with effect levels down to about 0.01  $\mu\text{g}/\text{kg}$ ) are: immune system damage; impaired reproduction/birth defects; increased incidence of tumours; and, increased induction of certain enzymes. These effects are not limited to TCDD. They can also be caused by high doses of the 16 other dioxins and furans of concern depending on their toxicity relative to TCDD.

The no-observed-adverse-effect-level (NOAEL) for the most sensitive toxic endpoints (cancer and reproduction) in rats is approximately 1 nanogram per kilogram of body weight per day.

Studies have been done on people who have been accidentally exposed to high levels of dioxins and furans, either as a result of improper waste disposal at work or from eating contaminated cooking oil. Chloracne, a skin disorder, is the most common human health effect. Extreme exposures also lead to other effects on the skin, liver, immune system, reproduction system, senses and behaviour.

## 2. DOSE-RESPONSE INFORMATION/CURRENT EXPOSURE GUIDELINES

The uncertainties surrounding the potential toxicological effects of environmental dioxins and furans on communities have influenced significantly the methodologies used to set guidelines and permissible exposure levels. As previously noted, the adoption of reasonably conservative assumptions is warranted in this context in order to provide sufficient protection of public health. This section summarizes various health criteria values, that is, exposure guidelines and dose-response information, primarily those that Ontario has proposed and consider appropriate for permitting, assessing, and characterizing risks associated with various exposures. Dioxins and furans are treated differently than substances in the other appendices, since Ontario has been involved for several years in the development of guidelines with national and international agencies and a consensus has developed. Some of the guidelines of other agencies are included as well for perspective purposes. Potential exposures to dioxins and furans are evaluated in section 3 and the risk characterization is presented in section 4.

The regulation of TCDD, a substance with carcinogenic properties, requires some understanding of its effects and its mode of action. TCDD is not genotoxic in the accepted sense. It does not react with or bind to genetic material and tests negatively in standard *in vitro* tests of mutagenicity. Most of its noncancer toxic responses are receptor-mediated. Several studies indicate that TCDD acts only as a promoter of cancer and not as a complete carcinogen. NOAELs have been observed for most toxic endpoints including cancer. Other toxic endpoints, e.g., reproductive and developmental toxicity and immunotoxicity appear to be at least as sensitive as the cancer endpoint. Based on these considerations, the current MOEE total exposure limit was published in 1985 (MOE, 1985). MOEE determined a tolerable daily intake (TDI) for TCDD or its toxicity equivalent (TEQ) of 10 picogram TEQ / kg body weight.

The federal government adopted this TDI under CEPA in 1990. The same TDI was also adopted by the World Health Organization in 1990.

### 2.1 International Toxicity Equivalency Factors (ie. TEFs)

Major environmental media (air, water and soil/sediment), industrial and municipal releases, and biological media such as food contain varying mixtures and concentrations of individual PCDD and PCDF congeners<sup>1,5,6</sup>. Regulatory practices to date have focused on protecting the public by controlling exposure to TCDD, the most toxic isomer. This approach may not provide adequate protection since TCDD is not the most abundant isomer and the toxicity of other isomers in the PCDD and PCDF mixtures that people are exposed to is not addressed. Although current knowledge of structure-activity relationships and the relative toxicities for PCDD and PCDF is quite limited, it does permit, in a preliminary fashion, the ranking of individual isomers relative to TCDD. The International Toxicity Equivalency Factor (I-TEF) scheme, a relative ranking approach proposed by NATO-CCMS report No. 176<sup>3</sup> has received acceptance by various agencies worldwide (U.K. (1989), USA (1989), Canada (1990)). These I-TEF are based on current scientific information (ie. NATO-CCMS report # 178<sup>4</sup>), and are subject to change as new data become available. As presented in Table A, this I-TEF scheme requires isomer-specific information so that the amounts of 2,3,7,8-substituted isomers may be quantified and the appropriate factors applied to generate TCDD toxicity equivalents (TEQ).

### 2.2 Air Guidelines and Other Route Guidelines

Ontario has been developing guidelines for dioxins and furans since 1981. Guidelines were set for sportfish consumption (1981) and ambient air quality (1983). The ambient air quality guideline, set in 1983, was one of the first air guidelines established for dioxins. Conservatively, it assumed that all dioxins were as toxic as TCDD. Furans, including all furans as a group, were assumed to be 1/50th as toxic as TCDD.



Since 1985, the TDI has been used as the basis for setting guidelines (interim drinking water guideline for dioxins and furans, 1986; revised sportfish consumption guideline, 1991; CCME interim soil quality guidelines, 1991; interim ambient air quality criterion, 1994). A package of revised guidelines for all environmental media will be submitted to the Advisory Committee on Environmental Standards (ACES) for public review in 1994. Table 1 lists existing and proposed exposure guidelines currently in use in Ontario. Air quality standards and guidelines used by a variety of agencies are provided in Table 1.a.

**Table A: International Toxicity Equivalency Factors for the 17 dioxin and furan isomers of concern (NATO-CCMS, 1989).**

Isomer of Concern	I-TEF
2,3,7,8-TCDD	1.0
1,2,3,7,8-P5CDD	0.5
1,2,3,4,7,8-H6CDD	0.1
1,2,3,7,8,9-H6CDD	0.1
1,2,3,6,7,8-H6CDD	0.1
1,2,3,4,6,7,8-H7CDD	0.01
1,2,3,4,6,7,8,9-OCDD	0.001
2,3,7,8-TCDF	0.1
2,3,4,7,8-P5CDF	0.5
1,2,3,7,8-P5CDF	0.05
1,2,3,4,7,8-H6CDF	0.1
1,2,3,7,8,9-H6CDF	0.1
1,2,3,6,7,8-H6CDF	0.1
2,3,4,6,7,8-H6CDF	0.1
1,2,3,4,6,7,8-H7CDF	0.01
1,2,3,4,7,8,9-H7CDF	0.01
1,2,3,4,6,7,8,9-OCDF	0.001



Table 1. SUMMARY of HUMAN EXPOSURE GUIDELINES CURRENTLY IN USE IN ONTARIO

Type of Guideline	Units	Calculated "Allowable" Intake (a) pg of: .... /day (b) (mg/kg/day)
Tolerable Daily Intake (Existing value)	10 pg TEQ / kg / day	Adults (70 kg): 700 (of: TEQ) Child (15 kg): 150 (of:TEQ)
Ontario Drinking Water Objective (Existing value)	15 pg TEQ / L	22.5 (of: TEQ) ( $3.2 \times 10^{-10}$ )
Interim Ambient Air Quality Criterion <sup>20</sup>	5 pg TEQ / m <sup>3</sup>	100 (of:TEQ) ( $1.4 \times 10^{-9}$ )
Provincial Water Quality Guideline (Existing value)	0.02 pg TCDD / L; 0.2 pg TCDF / L	
Sportfish Consumption Guideline (Existing value)	15 pg TEQ / g	
Agricultural Soil Limit (Proposed value)	10 pg TEQ / g	
Residential Soil Limit (Proposed value)	1000 pg TEQ / g	
<p>(a) These "Allowable" intakes are calculated for the purposes of this report to allow comparison of exposures to guidelines on a common basis (ie. intake /day). They do not imply that the guidelines be defined or formulated in this fashion, now or in the future. The intakes were computed by assuming, where applicable, an adult weight of 70 kg, a breathing rate of 20 m<sup>3</sup>/day, a water intake of 1.5 L/day. In all cases 100 % bioavailability of the intake was assumed.</p> <p>(b) Specific way of treating dioxin and furan mixtures(eg. using the international toxic equivalent approach - 'TEQ' approach, or other) are included in brackets following the concentration value.</p>		

Table 1.a. AIR QUALITY GUIDELINES USED BY OTHER AGENCIES

Agency	Units	Calculated "Allowable"Intake pg of:..../day (a)
EPA (1985) (10 <sup>-5</sup> lifetime risk) <sup>14</sup>	0.3 pg TCDD / m <sup>3</sup>	6 (of:TCDD)
California (1992)(10 <sup>-5</sup> lifetime risk)	0.3 pg TEQ / m <sup>3</sup>	6 (of:TEQ)
Connecticut (1988) <sup>17</sup>	1 pg TEQ / m <sup>3</sup>	20 (of:TEQ)
Massachusetts (1989) <sup>33</sup>	1.1 pg TCDD / m <sup>3</sup>	22 (of:TCDD)
Kansas <sup>18</sup>	3 pg TCDD / m <sup>3</sup>	60 (of:TCDD)
North Carolina <sup>18</sup>	3 pg TCDD / m <sup>3</sup>	60 (of:TCDD)

### 3. HUMAN EXPOSURE ASSESSMENT

#### 3.1 Inhalation

##### 3.1.1 Ambient Air Quality

Ambient levels of dioxins and furans have been measured at two fixed site stations in Windsor by the Ontario Ministry of the Environment. The measurement includes four years of data and 60 samples, each collected over a 24 hour period. Air concentrations of dioxins and furans will be discussed and presented in two different ways: concentrations as measured and concentrations in terms of 'toxic equivalents' (ie. using the international set of toxic equivalency factors). Further explanation of these measures of dioxins and furans can be found in the footnotes of Tables 2.a and 2.b.

Concentration levels (ie. as measured) of total dioxins and furans range from non-detectable to 53.7 pg/m<sup>3</sup>, with the median, mean (average), 90th percentile and 95th percentile levels being 5.0, 7.8, 16.4 and 24.5 pg/m<sup>3</sup>, respectively<sup>19</sup>.

'Toxic equivalent' (ie. TEQ) concentrations of dioxins and furans range from non-detectable to 1.7 pg TEQ/m<sup>3</sup>, with the median, mean (average), 90th percentile and 95th percentile levels being 0.13, 0.21, 0.45 and 0.71 pg TEQ/m<sup>3</sup>, respectively<sup>19</sup>.

It is possible to estimate the daily intake of dioxins and furans associated with these three measures of Windsor ambient air quality, recognizing that personal real exposures/intakes may be quite different as further discussed in section 3.1.2. Table 2.a and 2.b below, using the two different measures respectively, for dioxins/furans, shows the estimated intakes for two different receptors, i.e., an adult and a child. It should be noted that these intakes were calculated based on 24 hour exposures and assume 100% bioavailability by the inhalation route.

Table 2.a. Estimated Daily Intakes of Dioxins and Furans Associated With Ambient Air Quality in Windsor - Expressed as Total Concentrations Measured.

Air Quality Measure(a)	Concentration pg/m <sup>3</sup>	Adult(b) pg/day (pg/kg-day)	Child(b) pg/day (pg/kg-day)
Median	5.0	100.0 (1.4)	25 (1.7)
Mean	7.8	156.0 (2.2)	39 (2.6)
90th percentile	16.4	328.0 (4.7)	82 (5.5)

a) Based on 60, 24 hour average samples  
Concentrations in air are expressed as measured.

b) Assuming the following weights and inhalation rates per day (ie. per 24 hour period):  
Adult: 70 kg; 20 m<sup>3</sup>/day  
Child: 15 kg; 5 m<sup>3</sup>/day

**Table 2.b. Estimated Daily Intakes of Dioxins and Furans Associated With Ambient Air Quality in Windsor - Expressed as International Toxic Equivalents (I-TEQ).**

Air Quality Measure(a)	Concentration	Adult(b)	Child(b)
	pg I-TEQ/m <sup>3</sup>	pg I-TEQ/day (pg I-TEQ/kg-day)	pg I-TEQ/day (pg I-TEQ/kg-day)
Median	0.13	2.6 (0.04)	0.65 (0.04)
Mean	0.21	4.2 (0.06)	1.1 (0.07)
90th percentile	0.45	9.0 (0.13)	2.25 (0.15)

a) Based on 60, 24 hour average samples  
Concentrations are expressed in terms of 'International Toxic Equivalents' (I-TEQ). They were obtained using the International method for toxic equivalency factors and the percent of toxic isomers in ambient air as recommended by Birmingham, (Chemosphere, 1990, pp 815). For further details see section 2.1.

b) Assuming the following weights and inhalation rates per day (ie. per 24 hour period):  
Adult: 70 kg; 20 m<sup>3</sup>/day  
Child: 15 kg; 5 m<sup>3</sup>/day

### 3.1.2 Microenvironments

It is reasonable to assume that the daily dioxin/furan intakes associated with typical personal exposure patterns will be different from those based on fixed site monitoring data. With most of the substances on the Windsor focus list, this evaluation was based on various microenvironmental concentrations. For the purpose of scoping population exposures, the set of typical receptors in Table 3 below was considered. Examples of the receptor types and/or their characteristics are also included in Table 3. For dioxins/furans, Windsor-specific microenvironment and personal exposure concentrations were not available. As a surrogate, indoor concentrations acquired in other studies were used to represent the range of 'typical personal exposure' patterns. Studies were conducted by Kominsky<sup>34</sup> to determine the concentrations of PCDDs and PCDFs present as normal levels of background concentration in office buildings. The buildings were constructed in the mid-1960's and had no history of electrical transformer fires or failures. However, because of the limited number of measurements (ie. 16 samples collected in office workspaces) of dioxins and furans in indoor environments this data should be interpreted with care. The concentrations from these studies and the associated estimated daily intakes (in pg I-TEQ/day - international equivalents) are summarized in Table 4.

Table 3. Receptors With Typical Personal Exposure Patterns

NAME OF RECEPTOR TYPE	CHARACTERISTICS	NAME OF RECEPTOR TYPE	CHARACTERISTICS
Average Office Worker (Non-smoking)	Eg. - Typical office worker (Based on Windsor volunteers and US EPA TEAM study; not smoking at home)	High Outdoor Receptor	Eg. - Construction workers; - Bicycle couriers - Police - Long distance runners
Average Office Worker (Smoker Environment)	Eg. - Typical office worker (Based on Windsor volunteers and US EPA TEAM study; smoking at home)	High Indoor Receptor	Eg. - 'Shut-ins'- Invalids - Elderly, non-mobile
Average Youth	Eg. Special exposures at shopping malls and athletic facilities (pools) in addition to school;	High Commuting Receptor	Eg.- Bus drivers - Taxi drivers - Delivery/ Distribution Services
Average Child (Non-Smoker Home & No Exposure to Tobacco Smoke)	Eg. Similar to average office worker except 'School' replaces 'Office';	Active Receptor #1	Eg.- 7 hr/week in Bingo Hall or Bar
Average Child (Non-Smoker Home & Typical Exposure to Tobacco Smoke)	Eg. Includes typical times that children may be in proximity to tobacco smoke, outside the home, based on activity pattern studies;		
Average Child (Smoker Home with Exposure to Tobacco Smoke)	Eg. Child living in a house where there is a smoker		

Table 4. Estimated Daily Intakes of Dioxins/Furans Associated With Indoor Air Environments (ie. to represent 'Typical personal exposures' - see footnote 'c').

Indoor Air Environment(a)	Concentration pg TEQ/m <sup>3</sup>	Adult(b) pg TEQ/day (pg TEQ/kg-day)	Child(b) pg TEQ/day (pg TEQ/kg-day)
Range of measurements	0.003 - 0.33 (a)	0.06 - 6.6 (0.0009 - 0.09)	0.02 - 1.7 (0.001 - 0.1)
<p>a) Based on dioxin/furan measurements in office buildings by Kominsky<sup>24</sup> et al. The range of measured values (ie. minimum to maximum) from this study have been converted to toxic equivalents (TEQs) using the international toxic equivalency factors.</p> <p>b) Assuming the following weights and inhalation rates per day (ie. per 24 hour period): Adult: 70 kg; 20 m<sup>3</sup>/day Child: 15 kg; 5 m<sup>3</sup>/day</p> <p>c) Since 24 hr exposure to these indoor concentrations is assumed here, these estimates provide a 'worst-case' estimate for typical personal exposures.</p>			



In order to place the above inhalation exposures (ie. intakes) in Windsor in perspective, it is appropriate to compare to daily intakes that people who smoke may experience.

### 3.1.3 Smoking.

Gilman et al.<sup>21</sup> estimate that the potential exposure of a person who smokes 20 cigarettes a day is 0.5 pg TEQ/kg-d or 35 pg TEQ/d. This estimate is based on a 70 kg person inhaling 1 L of smoke per cigarette containing dioxins at a concentration of 1.8 ng TEQ/m<sup>3</sup> and an absorption of 100%. The estimate ignores the potential presence of furans and the differences between experimental protocol and actual smoking. It should be noted that these intake estimates are based on a single study and more recent information<sup>39</sup> indicates that intakes from cigarettes may be 10-fold less than the above estimates.

One cigarette will contribute 1.8 pg TEQ. Non-smokers who are heavily exposed to environmental tobacco smoke inhale the equivalent of 1/3 to 3 cigarettes per day or 0.6 to 5.4 pg TEQ/day (Blot and Fraumeni<sup>35</sup>). Vainio<sup>37</sup> states that the exposure of non-smokers to environmental tobacco smoke would be about 1% of that of active smokers or 0.4 pg TEQ/day, whereas Remmer<sup>36</sup> gives, as an upper limit, the equivalent of only 1/5 of a cigarette per day or 0.4 pg TEQ/day. Hiller<sup>38</sup>, quoting other authors, gives intakes ranging from a low of 0.001 cigarette equivalents (CE)/hr or 0.01 CE/day, assuming 12 hr exposure, to a high of 27 CE/day. The higher value is clearly anomalous as the range claimed by the other authors is 0.001 to 0.2 CE/hr. The lower value suggested by Hiller gives an intake of 0.4 pg TEQ/day.

It is also important to place the inhalation exposures (ie. intakes) in Windsor into perspective, relative to general exposures from other media (ie. see section 3.2).

## 3.2 Other Routes

In this section, possible non-inhalation routes of exposure (ie. ingestion and dermal) are estimated.

### 3.2.1 Ingestion of Food

The estimates of dioxins and furans are based generally on analyses of a relatively small number of food groups and samples. The latest assessment (Gilman et al.<sup>21</sup>) is based on earlier data (Birmingham *et al*<sup>22,23</sup>).

Estimates of intakes from food are given in Table B below.

It is possible also to estimate daily intakes by assuming that the levels of PCDD/PCDFs in human adipose tissue are in a dynamic equilibrium among uptake, retention and elimination. The calculated intake is 1.86 pg I-TEQ/kg bw-d (Gilman et al.<sup>21</sup>). The background exposure to PCDDs/PCDFs has been estimated to be 0.03-2.86 pg/kg-d (based on mean human adipose tissue concentrations of 6-12 pg/kg).

The intake for neonates is based on the ingestion 750 mL/d of breast milk (3% fat) containing 36.5 pg/g fat. Recent analyses of breast milk by the World Health Organization translates to intakes of 70 pg/kg bw-d (Gilman et al.<sup>21</sup>). This has been revised to 90 pg/kg bw-d or ≈13 pg 2,3,7,8-TCDD. It is estimated that the intake from this source is about 5% of the lifetime intake (Kello and Yrjänheikki<sup>25</sup>).



TABLE B. ESTIMATED INTAKES OF DIOXINS AND FURANS FROM FOOD.

REFERENCE	ESTIMATE INTAKE pg TEQ/kg bw-d;(pg TEQ/d) <sup>1</sup>			
	Adult <sup>2</sup>	Child <sup>3</sup>	Infant <sup>4</sup>	Neonate <sup>5</sup>
Gilman et al.(Ref. 21) <sup>6</sup>	0.49 - 2.0 (34-140)	1.18 - 4.78 (39-158)	2.6 - 10.7 (34-139)	165 (825)
Birmingham <i>et al</i> (Ref. 22) <sup>7</sup>	2.0; 1.7 (120)	-	-	-
Birmingham <i>et al</i> (Ref. 23) <sup>8</sup>	1.52; 1.31 (91)	-	-	-
<p>1. TEQ are based on the International Toxicity Equivalent Factors adopted in 1988. The lower end of all ranges assumes that a reported non-detectable value is equal to 0; the upper range assumes that a non-detectable value is equal to the limit of detection. The numbers in brackets are in units of pg TEQ/d.</p> <p>2. 17-70 yr; 70 kg</p> <p>3. 3-17 yr; 33 kg</p> <p>4. 0.5-3 yr; 13 kg</p> <p>5. &lt;0.5 yr; 5 kg.</p> <p>6. After Birmingham <i>et al</i><sup>22</sup>. Non-detects are assumed to be equal to the lowest detection limit.</p> <p>7. The intake value is based on a 60 kg adult; the number in italics is for a 70 kg adult.</p> <p>8. The intake value is based on a 60 kg adult; the number in italics is for a 70 kg adult. Where data were reported as non-detect, the residues are assumed to be absent.</p>				

Gilman *et al.*<sup>21</sup> also estimate that the lifetime average daily intake of a person consuming fish contaminated with PCDDs and PCDFs in excess of Canadian guidelines is 4.2-6.3 pg TEQ/kg-d, whereas for an average adult it is 1.9-4.0. These estimates are calculated by dividing the sum of the products of the estimated intakes for each life stage and the length of time for that stage by the 70 year exposure period.

The major sources of dioxins and furans in the food are milk, beef and eggs, with milk and dairy products being the largest source (25-50%). Generally, no T4CDD, P5CDD, H6CDD, T4CDF or P5CDF residues are found at the detection limit (0.1-7 pg/g) in food. Very small amounts of the higher chlorinated compounds are found in some foods, mostly near the detection limit (Birmingham *et al*<sup>22,23</sup>). Since animal and fish tissue tend to retain those congeners that are resistant to metabolism and excretion, the major isomers found are 2,3,7,8-substituted (Birmingham *et al*<sup>26</sup>).

The data reported in Birmingham *et al*<sup>22,23</sup> are based on a composite of both cooked and uncooked foods in the same category. The Ministry data is known to be based on analyses of raw foods; the National Health and Welfare food samples may be cooked. Ryan *et al*<sup>27</sup> state that foods, such as raw meats, were prepared in a manner suitable for consumption. Their data for six beef hamburger composites shows a mean concentration ( $\pm$ SD) of 0.19 $\pm$ 0.11 pg TEQ/kg bw-d, whereas Birmingham *et al*<sup>22,23</sup> give 0.36 and 0.23, respectively, for raw beef. The evidence is not sufficient to suggest any reduction in concentration from cooking.

### 3.2.2 Drinking Water

Dioxins and furans have been detected in Ontario drinking waters. Most analyses are less than the detection limit of 10 pg/L but range up to 46 pg/L of O8CDD. The estimated concentration is 0.07 TEQ/L, assuming that residues where data are reported as non-detect are present at the minimum reported detection limit. This is equivalent to an intake of 0.002 pg TEQ/kg-d or 0.1 pg TEQ/d for an adult (Birmingham *et al*<sup>22</sup>).

Gilman *et al.*<sup>21</sup> estimate the intakes to be the following:

adult	<0.01-0.05 pg TEQ/kg-d <0.7-3.5 pg TEQ/d
child	<0.01-0.07 <0.33-2.3
infant	<0.002-0.11 <0.03-1.4

Jobb *et al*<sup>28</sup> summarize the positive dioxin results from a survey of drinking water supplies in Ontario. The authors note that there were only 37 positive results out of 4347 and that the O8CDD congener accounted for 36 of the positives. The 2378-TCDD isomer was not detected in any sample. In 1985-86, there were 8 positives for O8CDD at Windsor, ranging from 22 to 63 pg/L, which is the equivalent of 0.02 to 0.06 pg TEQ/L. There is one value of 40 pg/L for the T4CDD congeners. The mean concentration cannot be calculated exactly since the majority of values are less than the detection limit of 3-8 pg/L.

### 3.2.3 Soil

PCDD/PCDF analyses of the 0-5 cm layer of soil were done in 1989 and 1990 for 18 urban and 7 rural samples (Gizyn<sup>29</sup>). The analyses were for isomer groups and are not isomer specific. Five of the 1989 urban stations were re-sampled in 1990. The concentrations in the repeat samples differed by as much as 100-fold, depending on the isomer groups and stations.

Because the analyses were not isomer specific, the factors proposed by Birmingham<sup>26</sup> to calculate the proportion of 2,3,7,8-substituted isomers in an isomer group were used together with the International Toxicity Equivalency Factors (ie. Table A) to calculate the toxic equivalents. The median concentrations for the 1990 analyses (12 urban, 4 rural) were used. The median calculated from the rural values is uncertain because of the large spread in concentrations. The medians for each isomer group and the toxic equivalents are given in Table C below.

The median total TEQ for the urban samples is 4.1 pg/g and 3.9 pg/g for the rural.

A reasonable estimate for the amount of ingested soil and dust is 80 mg/d for children and 20 mg/d for adults (MOE<sup>30</sup>; Appendix 1), although values as low as 0 for children <1 y, 40 mg/d for children 1-6 y and 10 mg/d for persons > 6 y have been used (Sheehan *et al*<sup>31</sup>). Using the MOE soil ingestion values, the intakes from soil in Windsor are:

	<u>Urban</u>	<u>Rural</u>
adults:	0.082 0.0012	0.078 pg TEQ/d 0.0011 pg TEQ/kg-d
children:	0.33 0.010	0.31 pg TEQ/d 0.0095 pg TEQ/kg-d

TABLE C. CONCENTRATIONS OF DIOXINS AND FURANS IN WINDSOR SOIL.

ISOMER GROUP	PROPORTION FACTOR <sup>1</sup>	I-TEF <sup>1</sup>	CONC. URBAN pg/g	TEQ URBAN pg/g	CONC. RURAL pg/g	TEQ RURAL pg/g
TCDD	0.1	1.0	5.3	0.53	2.6	0.26
P5CDD	0.1	0.5	6.3	0.32	5.3	0.27
H6CDD	0.3	0.1	10.5	0.32	25	0.75
H7CDD	0.6	0.01	41	0.25	58	0.35
O8CDD	1.0	0.001	175	0.18	410	0.41
				1.6		2.0
TCDF	0.1	0.1	29	0.29	20	0.20
P5CDF <sup>2</sup>	0.15	0.5	14.5	1.1	7	0.53
	0.15	0.05	14.5	0.11	7	0.05
H6CDF	0.5	0.1	16	0.80	15	0.77
H7CDF	0.5	0.01	34	0.17	53	0.27
O8CDF	1.0	0.001	22	0.02	27	0.03
TOTAL				2.5		1.9

- NOTES: 1. Information from tables 2 and 1, respectively, in Birmingham<sup>26</sup>  
2. Since there are two I-TEF values for P5CDF, the calculation is done twice.

These estimated intakes are lower than the Gilman *et al.*<sup>21</sup> estimates of 0.01 pg TEQ/kg-d for adults, 0.027-0.03 for children and 0.34-0.38 for infants. Birmingham *et al.*<sup>22</sup> gives a figure of 0.02, based on a mean soil concentration of 49 pg TEQ/g.

A recent paper by Copeland *et al.*<sup>24</sup> has looked at intake and uptake of dioxins and furans at a former wood treatment site, using a Monte Carlo analysis. They point out that the oral bioavailability of non-octa congeners is in the range of 39-49%, but only 2.5-5% for octa congeners. The octa congeners at Windsor (ie. see Table C above) make up about 10% of the total TEQs; therefore, the lower bioavailability does not make a major difference in estimating the uptake. The uptake is about 50% of the intakes calculated above.

### 3.2.4 Dermal

#### 3.2.4.1 During Showering and Bathing

Since dioxins and furans partition strongly to particulates in the water supply, the dermal uptake during showering and bathing is expected to be minimal.

#### 3.2.4.2 Contact With Soil and Dirt

Experiments on the dermal absorption of 2,3,7,8-TCDD *in vitro* with rat and human skin and *in vivo* with rats are discussed in an EPA report on dermal exposures<sup>32</sup>. The recommended percent of applied dose that is absorbed in 24 hr is 0.1-3%. Since the percent absorbed varies inversely with the organic content of the soil, the lower end of the range is recommended for soils with high carbon content and the higher end for soils with low carbon content. Copeland *et al*<sup>24</sup> recommend a range of 0.1-2%.

The most appropriate daily loading of soil on exposed skin is estimated to be 1.8 mg/cm<sup>2</sup> (range 0.5 - 2.8). The exposed area is taken to be 1580 cm<sup>2</sup> for a child and 1980 for an adult, or basically the hands and arms (Sheehan, P.J. *et al*<sup>31</sup>).

Taking the amount absorbed as 0.1 - 3% for all dioxin and furan congeners and using the average soil concentrations of 4.1 pg TEQ/g for the urban samples and 3.9 pg TEQ/g for the rural (s.3.2.3) or a loading of 7.4-7.0 fg/cm<sup>2</sup>, the amounts absorbed through the skin in 24 hr is:

adults:	0.014-0.44 pg TEQ/day
children:	0.011-0.35 pg TEQ/day

It is unlikely that the skin is as contaminated in winter as in summer or that the hands and arms are covered by dust and soil 24 hours a day. Therefore, the amount absorbed daily when averaged over the period of a year would be less than the uptakes calculated above.

## 4. RISK CHARACTERIZATION AND PERSPECTIVES

Exposures, expressed as daily intakes in units of pg TEQ/day, were assessed in section 3. Inhalation, ingestion and dermal routes of exposure were considered. Table 5 below summarizes the daily intakes (or ranges of daily intakes) of dioxins/furans, for adults and children, estimated in section 3. It should be noted that in section 3, the intakes for inhalation and sometimes for ingestion assumed 100% bioavailability. The intake for dermal exposures are amounts absorbed systemically and hence already include bioavailability considerations. Table 5 has two columns for both adults and children. The first set of columns (ie. '100 % Bioav') give the intakes with 100 % bioavailability having been assumed; the second set (ie. 'Bioav. Incl.'), gives intakes for which bioavailability has been taken into consideration (ie. if information was available as noted in the footnotes). This second set of columns should allow a better deduction of the relative importance of various exposure routes. As far as comparison to exposure guidelines and intakes associated with cancer risk, the intakes in the first set of columns of Table 5 will be used since the exposure guidelines are also expressed as intakes for which we have assumed 100 % bioavailability.



To characterize risks, the various exposure guidelines discussed in Section 2 are compared to the estimated exposures from inhalation and other routes as discussed in Section 3. Because of the assumptions, uncertainties and ranges of values available from both exposures (see Table 5) and the various exposure guidelines (see Table 1 and Table 1.a), risk characterization is most appropriately done by comparison of ranges of values.

Table 6 below provides a graphic representation of this comparison of exposures, exposure guidelines and risk estimates based on pg (or pg of TEQ) intake/day (ie. 'INTAKE in Picograms or pg TEQ per day' increasing upwards on the vertical scale).

The middle section of Table 6, "Exposures", depicts the exposures calculated in Section 3, expressed as intake/day (ie. pg TEQ/day). The exposures depicted are: *Outdoor Air Quality* - the exposure from spending 100 % of the day outdoors; *Typical Outdoor Exposure* - the exposure from three hours only outdoors, provided for perspective on the contribution to risk solely from contaminants present in outdoor air; *Typical Personal Exposures* - the range of exposures associated with 'personal activity patterns'. For dioxins & furans, surrogate indoor air values were used because of the lack of Windsor-specific data. It should be noted here, that since 24 hour exposures were assumed when using these surrogate indoor air concentrations, these estimates provide a 'worst-case' representation of 'typical personal exposures'. Exposure scenarios are included for adults and children, assuming 20 and 5 m<sup>3</sup>/day inhalation rates respectively. For 'outdoor air quality' (ie. 100% outdoor exposure) and for 'typical outdoor exposures' (ie. 3 hr) the ranges shown, bracket the lowest mean to the highest 90th percentile. For 'personal activity patterns' the range indicates the overall range of possible exposures (see s. 3.1.2 and Table 4). For perspective purposes, the exposures of smokers, directly from smoking activity is also depicted in this section.

The left section of Table 6, "Exposure Guidelines", expresses the various guidelines discussed in Section 2 in terms of calculated "allowable" intake/day for adults and children. The values are taken from Table 1 and Table 1.a. Within each type of guideline group (eg. outdoor air) ranges of exposure guidelines, when available, are indicated. Thus, ranges of Air Quality Guidelines (ie. 'Outdoor Air') and the Tolerable Daily Intake -TDI (ie. 'TOL. DAILY INTAKE'), 'allowed' from all exposure pathways, are shown. The interim MOEE air guideline(ie. expressed for the purposes of this table in terms of intake/ day) is also shown as a horizontal bar.

Based on the tabular analysis (Table 5) and the graphic risk characterization (Table 6), the following observations and deductions can be made:

#### Health messages:

- 1) It is apparent that the ingestion route dominates all other exposure routes for dioxins and furans. The inhalation route appears to be next in importance followed by the dermal route.
- 2) In terms of comparison to the Tolerable Daily Intake - TDI (ie. "TOL. DAILY INTAKE"), 'allowed' from all exposure pathways, the contribution associated with outdoor air quality exposure, with typical outdoor exposures and with personal activity patterns to the TDI are 1.3, 0.2 and 0.9 % respectively. These percentages are based on the highest estimated exposure values. The TDI level is considered to be purely health based and is protective against all chronic health effects including cancer. Therefore the possibility of long-term health effects is unlikely.
- 3) For a smoker, the inhalation exposure is dominated by the dioxins in cigarettes. It should be noted that



based on recent data the dioxins and furans in cigarettes may be 10-fold less than the estimates in this report.

4) Total ingestion exposures for adults and children (ie. 30 -163 pg TEQ/day; not shown in Table 6) are below the total tolerable daily intake 'allowed' for adults and children by the TDI guideline (ie. 700 pg TEQ/day; not shown in Table 6; see Table 1) and represents an  $\approx$  23 % contribution of the ingestion exposures to the TDI.

5) Dermal exposures (ie. 0.011 - 0.44 pg TEQ/day in Table 5) represent a negligible (ie.  $\approx$  0.1 %) contribution to the TDI via this pathway.

6) Based on points # 2,4 and 5 above, evaluating various routes of exposure, the combined exposure contributions to the TDI are less than  $\approx$  25%.

#### **Regulatory compliance messages:**

7) The risk characterization in Table 6 indicates that, for the inhalation receptor exposures considered:

- The exposures potentially associated with outdoor air quality, for adults, youth and children, fall in the lower 15% range of the air quality guidelines of various jurisdictions.
- Exposures associated with typical outdoor exposure (ie.3 hr) fall below the range of the air quality guidelines of various jurisdictions
- Exposures associated with personal activity patterns (ie. obtained from a 'worst-case' estimate, using surrogate indoor air values and assuming 24 hr indoor exposure) fall in the lower 10% range of the air quality guidelines of various jurisdictions.

It should be noted that these air quality guidelines may be of different types. Some are purely health based and some are regulatory and therefore may have been influenced by various risk management considerations. The regulatory guidelines may also have different uses (eg. judging the acceptability of air quality per se or judging the incremental addition by a source to the existing air quality).

8) All the inhalation exposures are below the interim MOEE air guideline (ie. when expressed in terms of international equivalents and in terms of 'tolerable' intake per day = 100 pg I-TEQ/day).

9) Ingestion exposures from drinking water (ie. <0.7 - 3.5 pg TEQ/day for adults and <0.3 - 2.3 pg TEQ/day for children in Table 5) are below the existing Ontario Drinking Water Objective (ie. 22.5 pg TEQ/day in Table 1). These drinking water-specific exposures and the Ontario Drinking Water Objective are not depicted in Table 6.

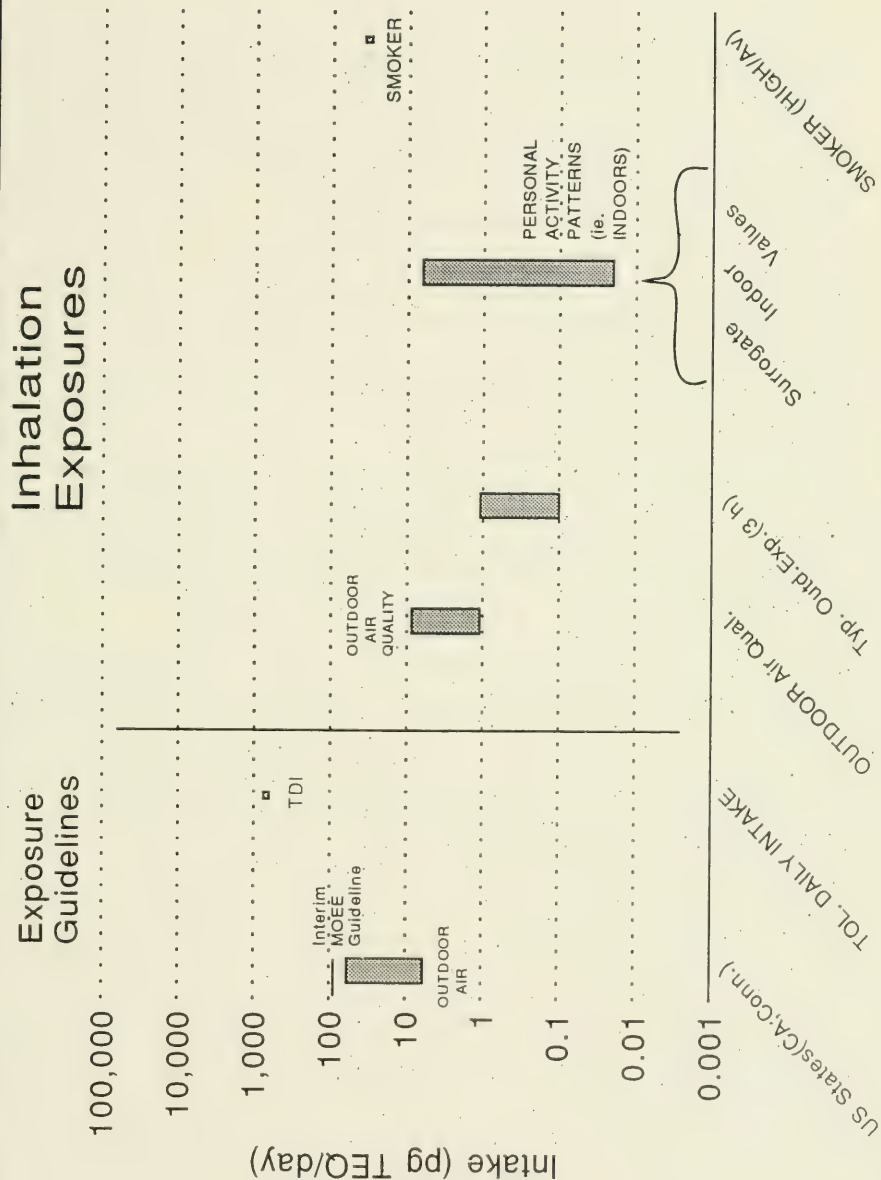
10) MOEE is presently reviewing the existing standards for dioxins and furans.

Table 5. Summary of Estimated Daily Intakes and/or Range of Intakes (in pg TEQ/day), from Various Exposure Pathways (ie. intakes, assuming 100 % bioavailability and intakes with bioavailability taken into consideration)

EXPOSURE PATHWAY		ADULT pg TEQ/day  (100 % Bioav.)	ADULT pg TEQ/day  (Bioav. Incl.)	CHILD pg TEQ/day  (100 % Bioav.)	CHILD pg TEQ/day  (Bioav. Incl.)
INHALATION	Outdoor Air Quality - Windsor (ie. 100 % outdoor exposure)(a)	4.2 - 9.0	1.6 - 3.3 (d)	1.1 - 2.25	0.4 - 0.8 (d)
	Typical outdoor exposure (ie. $\approx$ 3hr)(b)	0.5 - 1.1	0.2 - 0.4 (d)	0.1 - 0.3	0.04 - 0.1 (d)
	Typical personal exposures (ie. Table 4/Surrogate indoor values) (c)	0.06 - 6.6	0.02 - 2.4 (d)	0.02 - 1.7	0.007 - 0.6 (d)
	Smoker (e)	35	13 (d)		
INGESTION	Food	30 - 140	24 - 110 (f)	40 - 160	32 - 130 (f)
	Drinking water	<0.7 - 3.5	<0.6 - 2.8(f)	<0.3 - 2.3	<0.2 - 1.8(f)
	Soil	0.08	0.008 (g)	0.3	0.03 (g)
	TOTAL (Ingestion)	30 - 144	24 - 113	40 - 163	32 - 132
DERMAL	During showering/ bathing (h)	-	-	-	-
	Contact with soil & dirt		0.014 - 0.44		0.011 - 0.35
	TOTAL (Dermal)		0.014 - 0.44		0.011 - 0.35
<p>a.) Range of intakes is associated with the range of the 'mean' to '90th percentile' concentrations in outdoor air. It is to be noted that people are not exposed 24 hours to outdoor air. This estimation assumes 100 % exposure to outdoor air and is a measure of outdoor air quality per se and not of actual exposure.</p> <p>b.) Range of intakes calculated from the 'mean' to '90th percentile' concentrations in outdoor air and assuming a 'typical' outdoor air exposure of <math>\approx</math> 3 hr (ie. corresponding to breathing 2.5 m<sup>3</sup>/3hr for adults and 0.63 m<sup>3</sup>/3hr for children.</p> <p>c.) Range of intakes is estimated from the range of minimum to maximum measurements obtained from the workspace of office buildings (see Table 4). These were assumed to represent a 'worst-case' estimate (ie. since a full 24 hour exposure to indoor concentrations were assumed) of the range of intakes associated with 'typical personal exposure' patterns.</p> <p>d.) 37 % of dioxins on inhaled particulates are bioavailable (see s. 1.1).</p> <p>e.) The intake shown is the direct intake of an adult smoker from smoking activity (ie. 'smoking') only.</p> <p>f.) Up to 80 % of dioxins in food and drinking water can be absorbed (see s. 1.1)</p> <p>g.) The bioavailability of ingested soil is &lt; 10% (see s. 1.1).</p> <p>h.) Dermal uptake is minimal, since dioxins and furans partition strongly to particulates in water.</p>					

Table 6. DIOXIN/FURAN RISK CHARACTERIZATION in WINDSOR  
 Ranges of exposure guidelines and exposures

1990X



#### Summary and recommendations:

- ♦ All the inhalation exposures contribute less than 2 % to the tolerable daily intake (TDI). Therefore the possibility of long-term health effects from inhalation exposures are not expected.
- ♦ Based on combined exposures from inhalation, ingestion (ie. the dominant exposure for dioxins and furans) and via skin absorption, the sum of these exposures is less than approximately a 25 % contribution to the TDI. Therefore, the possibility of long-term health effects from all exposures to dioxins and furans is unlikely.

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**APPENDIX 10**  
**RISK ANALYSIS FOR MERCURY**



**APPENDIX 10**  
**RISK ANALYSIS FOR MERCURY**

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## MERCURY

### DESCRIPTION and SOURCES of MERCURY.

Mercury is ubiquitous in the environment, being found in three forms (ie. valence states): metallic or elemental mercury ( $\text{Hg}^0$ ), mercurous mercury ( $\text{Hg}^{+1}$ ) and mercuric mercury ( $\text{Hg}^{+2}$ ). In the metallic form, mercury is a shiny, silver-white, odorless liquid with a metallic taste. Mercury can combine with other elements, such as chlorine, carbon, or oxygen, to form mercury compounds. These compounds are called "organic mercury" if they contain carbon, and "inorganic mercury" if they do not. All forms of mercury are considered poisonous. One organic form of mercury, methylmercury, is of particular concern because it can build up (bioaccumulate) in fish.

Mercury is used in thermometers, barometers and other pressure sensing devices. Batteries containing mercury are used in a variety of devices (eg. cameras, toys, portable radios, smoke alarms, etc.). In addition, electric or mercury lamps are used for outdoor lighting (including floodlights and streetlights), for motion picture projection, for health treatment and photography. Mercury is used as a catalyst in the chlorine and caustic soda industry and in the production of vinyl chloride. Other uses include, paint pigments, refining/lubricating oils and dental amalgams.

Mercury is released to environmental media by both natural processes and anthropogenic sources. Mercury is found in all classes of rocks. The major source of atmospheric mercury has been reported to be global degassing of mineral mercury from the lithosphere and hydrosphere. Anthropogenic releases of mercury to the atmosphere occur from the mining and smelting of mercury ores, industrial processes involving the use of mercury, and combustion of fossil fuels, primarily coal. Other potential emission sources include chlorine-alkali manufacturing facilities, copper and zinc smelting operations, paint applications, waste oil combustion, municipal waste and medical waste incineration.

### 1. HAZARD IDENTIFICATION

An extensive review on the toxicology, human epidemiology, environmental fate, and properties of mercury was published recently by the Agency for Toxic Substances and Disease Registry (ATSDR) of the US Department of Health and Human Services, Public Health Service<sup>1</sup>. The review, which encompasses past and recent findings obtained from a detailed literature search, provides an excellent integrative and interpretative evaluation of the mercury issue as related to its potential health effects on humans following exposure through various environmental media. As it is the scope of the current document to provide a general, although comprehensive updated overview on the toxicology of mercury, excerpts of the recent ATSDR document were adapted in the following sections to summarize the information considered to be of relevance for the Windsor study. A more detailed discussion of the health effects of mercury can be obtained by consulting various references contained in section 5<sup>1-5</sup>.

#### 1.1 Absorption and Metabolism

Mercury exists in a large number of physical and chemical states which play an important role in the biogeochemical cycling and, thus, the environmental fate of this element. Mercury may be found in organic and inorganic forms; in the solid, aqueous, and vapor phases; and in some components of the food chain. As a result, humans are likely to be exposed to mercury, simultaneously or sequentially through different pathways.

Elemental mercury ( $\text{Hg}^0$ ) is the predominant form of mercury present in the atmosphere and,

consequently, is considered the most relevant for pulmonary exposure. The mercuric ( $\text{Hg}^{+2}$ ) and, to a lesser extent, the mercurous ( $\text{Hg}^{+1}$ ) ions are mainly present in the aqueous phase and may contribute to oral intake of the element. On the other hand, organic mercury, such as the mono- and dimethyl mercury forms which can be produced by certain microorganisms, are considered to be among the predominant chemical species of mercury in some foods (e.g., fish and fish products)<sup>5</sup>.

In conjunction with the multimedia/multipathway nature of mercury, the various physical and chemical forms of this element may also have different toxicological properties as a result of pharmacokinetic and metabolic differences. In fact, although the toxicity of the various forms of mercury seems to be related to cationic mercury ( $\text{Hg}^{+2}$ ) *per se*, it is the solubility, biotransformation, and tissue distribution of the different species of Hg that, ultimately, will determine the target organs and, possibly, the mechanisms of action. These parameters are influenced by the valence state of mercury and the associated anionic components, when present<sup>3</sup>. Consequently, the assessment of potential health effects induced by environmental mercury must integrate knowledge about the various exposure pathways and the associated chemical and physical forms of the element in these media (speciation).

There are limited quantitative data on the absorption of metallic mercury vapors ( $\text{Hg}^0$ ) by humans after inhalation exposure, although it is the most common route of inorganic mercury uptake<sup>3</sup>. Because of its high lipophilic properties, metallic mercury ( $\text{Hg}^0$ ) is readily absorbed (100% absorption of the inhaled vapor) across the alveolar membranes of the lungs and diffuses into blood<sup>1</sup>. On the other hand, no studies were located regarding the pulmonary bioavailability of organic mercury in both humans and animals, although indirect evidence suggest that uptake may be quantitatively important<sup>1</sup>. Limited data also suggest that oral absorption of inorganic mercury is poor and is estimated at approximately 0.1% for metallic mercury ( $\text{Hg}^0$ ), and 7% for an ingested dose of divalent mercury ( $\text{Hg}^{+2}$ ). In contrast to these values, it has been reported that up to 95% of a tracer dose of aqueous methylmercury nitrate was absorbed in humans<sup>1,4</sup>, thus indicating the high lipophilic nature of organomercurial compounds. Little data is available on the dermal absorption of the various forms of mercury although ACGIH<sup>13</sup> and ATSDR<sup>1</sup> indicate that it is considered relatively insignificant for ionic mercury, and moderate for elemental mercury.

Following its absorption in the systemic circulation, mercury is rapidly translocated to various organs and tissues, with high concentrations generally being observed in the kidneys. As previously mentioned, distribution profiles are influenced by the chemical form of the element, as suggested by the higher binding capacity of ionic mercury to plasma proteins, and the propensity of organomercurial compounds to concentrate in red blood cells as a result of their weak binding to hemoglobin. Generally, higher amounts of elemental ( $\text{Hg}^0$ ) and organic mercury are transferred through the placenta and blood-brain barriers, while protein-bound inorganic mercury are more likely to be filtered through kidney glomerules and retained in tubular cells<sup>3</sup>. Retention in the brain and the fetus is favoured by the oxidation of organic mercury to divalent mercury ( $\text{Hg}^{+2}$ ), which subsequently binds to sulfhydryl and/or thiol groups. Blood-brain ratios in the range of 5 to 1 have been reported in primates, and a comparable range has been suggested for humans<sup>4</sup>. However, several other oxidation-reduction mechanisms have been shown to occur in tissues<sup>1</sup>, and the influence of enterohepatic cycling and secondary redistribution of water-soluble organic forms of mercury<sup>4</sup> must be accounted for when assessing the pharmacokinetics of this chemical.

The elimination of mercury proceeds *via* the three main routes, depending on its chemical form. Inorganic mercury is excreted in the urine and feces, while unmetabolized organic mercury is excreted predominantly *via* the feces, in humans. Small amounts of elemental mercury ( $\text{Hg}^0$ ) are also eliminated *via* expired air<sup>1,3</sup>. Based on observations of six subjects that have ingested a single low dose of mercury, and on Iraqi mothers exposed for many months, the biological half-life of mercury in blood has been estimated at approximately 50 days (40-105 days)<sup>4,13</sup>.

## 1.2 Toxicology

Definitive data on the mechanisms of action for mercury and its compounds are limited, although it is believed that the high affinity and binding of the mercuric cation ( $\text{Hg}^{+2}$ ) to protein-containing sulfhydryl and/or thiol groups could be one of the main etiologic factor<sup>1</sup>. As previously noted, the adverse health effects induced by mercury compounds are somewhat influenced by the route of exposure.

Inhalation of metallic mercury vapors ( $\text{Hg}^0$ ) has been associated with systemic toxicity in both animals and humans. Under acute, high exposure levels ( $1\text{--}100\text{ mg/m}^3$ ), respiratory, cardiovascular, neurological, hepatic, renal, and gastrointestinal effects have been demonstrated in animals<sup>1</sup>. In situations of chronic, low concentration exposure scenarios, however, the major target organs of  $\text{Hg}^0$ -induced toxicity are the kidney and central nervous system<sup>1,5</sup>. Low Observed Adverse Effect Levels (LOAELs) for neurological disturbances have been reported to be in the range of  $50\text{--}100\text{ ug Hg/m}^3$  in humans<sup>1,4</sup>. According to the recent ATSDR<sup>1</sup> summary document, no studies were located on effect levels concerning inhalation exposure to other inorganic compounds (mercuric or mercurous salts, oxides, etc.), and limited information is also available for organic compounds.

Contrary to the inhalation route, a substantial amount of information is available on the effects of ingested mercury in humans and experimental animals<sup>1,3,4</sup>. As with inhalation exposure to metallic mercury vapors, major target organs of toxicity following oral exposure to inorganic and organic mercury are the kidney (nephrotic syndrome, glomerular and tubular pathologies), and the central nervous system (functional neurotoxicity and neuropathological changes). Oral exposure to mercury, especially the organic mercury form, has also been observed to result in adverse developmental effects in humans and experimental animals.

In this regard, the outbreaks of severe poisoning that occurred in Japan (Minamata Bay) and Iraq<sup>3</sup> in the 50's and early 70's, respectively, revealed important characteristics of the action of methylmercury in human adults. Clarkson<sup>4</sup> has summarized these effects as follows: 1) overt signs and symptoms usually take weeks or months to manifest; 2) all the signs and symptoms are due to selective damage to the nervous system; and 3) the brain is the primary target organ as manifested by loss of neuronal cells in the visual cortex and the granule layer of the cerebellum. Reasons for these specific effects (latent period and focal damage), however, are not known yet. Of major importance for the assessment of neurological effects induced by mercury in humans has been the establishment of dose-response relationships for various end-points. Hence, a dose-related increase between the severity of the effect and the concentration of mercury in hair is available for pathologies progressing from paresthesia, to ataxia, dysarthria, deafness, and finally death<sup>4</sup>. As the amount of mercury in blood (from recent and past exposures) may be readily estimated from the concentration of mercury in hair, and that pharmacokinetics modeling allows relationships between blood mercury and exposure to be established, then a direct quantitative cause-effect relationship for various neurological effects and exposure to mercury is possible.

The Iraqi and Japanese outbreaks have also revealed the capacity of mercury to induce prenatal toxicity in humans, an observation that was later confirmed by experiments in laboratory animals<sup>1,3,4</sup>. Clinical findings have included reports of infants suffering from severe brain damages in mothers exposed to methylmercury during pregnancy. Several cases of mental and psychomotor retardation were also noted<sup>4</sup>. Generally, these effects were seen predominantly in male infants, a consequence which most probably seems to be associated with the higher sensitivity of males to mercury-induced mitotic arrest of dividing neuronal cells<sup>4</sup>. Finally, in his recent discussion, Clarkson<sup>4</sup> indicates that, based on dose-response data, the fetus may be 5-10 times more sensitive than the adult to brain damage from methylmercury.

Finally, some evidence obtained from experimental studies in laboratory animals has also suggested that both organic and inorganic mercury could affect the cardiovascular system (increase in systolic blood pressure and cardiac contractility, decreased baroreflex sensitivity), gastrointestinal system (increased



incidence of forestomach hyperplasia in male rats chronically exposed), adrenocortical function (increase in adrenal and plasma corticosterone levels), immunological system (e.g., lymphoproliferative response suppression, decrease in antibody response, etc.), and reproductive function (e.g., resorption, spontaneous abortions, decreased litter size, etc.).

Of importance for public health implication is the genotoxic status of mercury. In this regard, no information is reported by the US EPA in their Integrated Risk Information System (IRIS)<sup>6</sup> database. ATSDR<sup>1</sup> reports that there is inconclusive evidence that occupational exposure to metallic mercury and to organic and inorganic mercury compounds, primarily through inhalation, causes structural (clastogenicity) and numerical (aneuploidy) chromosome damages in human lymphocytes as observed in occupationally exposed workers. These same conclusions apply to the case of subjects orally exposed to mercury. Therefore, the evidence of genotoxic potential of mercury in humans is inconclusive. Experimental *in vitro* and *in vivo* studies, on the other hand, provide some evidence of the capacity of inorganic and organic mercury to interact with DNA in mammalian and bacterial cells (for review see ATSDR<sup>1</sup>). Recently, the World Health Organization (WHO), International Programme on Chemical Safety (IPCS)<sup>14</sup>, after reviewing the mutagenicity of methyl mercury, concluded on the positive genotoxicity of this compound in standardized *in vitro* tests.

There is no evidence from epidemiological studies that indicates inhalation and oral exposure to inorganic and organic mercury produces cancer in humans<sup>1</sup>. However, recent studies conducted by the National Toxicology Program (NTP)<sup>1</sup> indicates that lifetime gavage exposure to mercuric chloride (HgCl<sub>2</sub>) induces an increased incidence of forestomach squamous cell papillomas in low-dosed males, and a marginal increase in the incidence of thyroid follicular cell carcinomas in the high-dosed male rats. Furthermore, renal tubule tumors were evident in 3 of the 49 high dosed-male mice. The implications of these findings for risk assessment are not clear yet in view of a lack of dose-response relationship for these effects. Mercury (inorganic) is currently classified in Group D (not classifiable as to human carcinogenicity) by the US EPA<sup>6</sup> on the base of unavailable human data, and inadequate animal and supporting data. No information on the carcinogenic potential of mercury has been disseminated by the International Agency of Research on Cancer (IARC) and the NTP.

## 2. DOSE-RESPONSE INFORMATION/CURRENT EXPOSURE GUIDELINES

This section summarizes various health criteria values, that is, exposure guidelines and dose-response information that leading regulatory agencies (and other relevant sources) have proposed and consider appropriate for permitting, assessing, and characterizing risks associated with various exposures. Potential exposures to mercury are evaluated in section 3 and the risk characterization is presented in section 4.

### 2.1 Air Guidelines

#### 2.1.1 Chronic, Non-Carcinogenic Effects

The US EPA's Integrated Risk Information System database<sup>6</sup> notes that the inhalation Reference Concentration (RfC) for inorganic mercury is under review, and no RfC for organic mercury (as methyl mercury) is available at this time. On the other hand, the Office of Research and Development of the US EPA suggests in its 1992 edition of the Health Effects Assessment Summary Tables (HEAST)<sup>7</sup>, an RfC for elemental mercury (Hg<sup>0</sup>) of  $3 \times 10^{-4}$  mg/m<sup>3</sup> set to prevent neurotoxic effects. It is noted, however, that this value is under review and, consequently, subject to change. EPA defines an RfC as an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime.

The California Air Pollution Control Officers Association (CAPCOA), as reported in their California Air Toxics "Hot Spots" Program, Risk Assessment Guidelines<sup>8</sup>, has proposed for total mercury an inhalation chronic AEL (Acceptable Exposure Level) of  $3 \times 10^{-4}$  mg/m<sup>3</sup>, based on the 1991 US EPA HEAST report. The AEL is used for the evaluation of the potential noncancer adverse health effects of long-term (chronic) exposures.

The New York State Department of Environmental Conservation (NYSDEC) has proposed in its Guidelines for the Control of Toxic Ambient Air Contaminants<sup>10</sup>, an Annual Guideline Concentration (AGL) of  $2.4 \times 10^{-2}$  ug/m<sup>3</sup> for methyl mercury, derived based on the occupational Threshold-Limit-Value, Time-Weighted-Average (TLV-TWA) of the American Conference of Governmental Industrial Hygienists (ACGIH). Similarly, an AGC of  $3 \times 10^{-1}$  ug/m<sup>3</sup> has been derived from the same source for inorganic mercury. Interestingly, NYSDEC has classified methyl mercury and inorganic mercury in the "High Toxicity Air Contaminants" and "Moderate Toxicity Air Contaminants", respectively.

Several other US states have adopted Acceptable Ambient Air Concentrations (AAACs) for mercury. The values summarized in the 1993 edition of the ATSDR<sup>1</sup> toxicological profile for mercury, however, are not documented as to their origin and applicability (e.g., nature of the toxicological end-point, applicable to organic or inorganic mercury). Furthermore, widely varying averaging times are presented, with different AAACs having been allocated by one or more jurisdictions to 24 hours and annual values. The rationale for this allocation was not discussed. Therefore, in order to prevent confusion when comparing AAACs to values proposed by other jurisdictions/regulatory agencies, annual values were retained. In this respect, annual values proposed by various US states cover a range of 3 orders of magnitude, from the 0.01 ug/m<sup>3</sup> proposed by the State of Montana, to the 12 ug/m<sup>3</sup> of the State of Vermont. Intermediate annual values of 0.024, 0.05 and 0.24 ug/m<sup>3</sup> have been proposed by the states of Kansas, Texas, and Montana, respectively.

The World Health Organization, in its 1986 Air Quality Guidelines for Europe<sup>5</sup>, has not recommended any ambient air guideline based on the argument that absence of quantitative information on the consequences of the deposition of atmospheric mercury precludes the determination of the associated potential health effects. This same *status quo* seems to prevail today in the WHO policy on atmospheric mercury<sup>1</sup>.

The Ontario Ministry of the Environment has proposed, in 1974, an Ambient Air Quality Criteria (AAQC) of 2 ug/m<sup>3</sup> for inorganic mercury. This was 1/25 of the ACGIH TLV available at that time. In 1974, an AAQC of 0.5 ug/m<sup>3</sup> for mercury alkyl compounds (as Hg) was proposed based, once again, on the then available TLV-TWA. Both these values are currently under review/update by the Ministry.

The occupational exposure limits for both organic and inorganic mercury have been updated recently by ACGIH<sup>13</sup>. In the case of inorganic mercury, ACGIH proposes a TLV-TWA of 50 ug/m<sup>3</sup> as Hg for mercury vapors (Hg<sup>0</sup>), and 100 ug/m<sup>3</sup> as Hg for aryl and other inorganic compounds. These values were set to prevent adverse health effects on the central nervous system. However, in view of the new data on the male reproductive effects and the demonstrated ability to show a biological threshold for preclinical changes by measurement of mercury in urine, the current TLVs for mercury vapor and aryl and inorganic compounds are being considered for reduction. For organic mercury compounds (alkyl), the proposed TLV-TWA is of 10 ug/m<sup>3</sup> based on the severity of the central nervous system effects. Similar values have been proposed for both classes of mercury compounds by the Occupational Health and Safety Administration (OSHA)<sup>13</sup>.

The above guidelines for atmospheric mercury are summarized in Table 1 below.



### 2.1.2 Carcinogenic effects

The evidence for the carcinogenicity of mercury in humans and animals is inconclusive.

### 2.3 Other Route Guidelines

The US EPA's Integrated Risk Information System database<sup>6</sup> notes that the oral Reference Dose (RfD) for inorganic mercury is under review. However, the Office of Research and Development of the US EPA suggests in its 1992 edition of the Health Effects Assessment Summary Tables (HEAST)<sup>7</sup>, an RfD for inorganic mercury of 0.3 ug/kg-day based on kidney effects in animals exposed orally. The later value is currently under review and subject to change. The IRIS database also reports an oral RfD of 0.3 ug/kg-day for methyl mercury based on a Low Observed Adversed Effect Level (LOAEL) for central nervous system effects of 3 ug/kg-day in humans (Uncertainty Factor = 10). A similar value is reported in the HEAST report<sup>7</sup>.

The California Air Pollution Control Officers Association (CAPCOA), as reported in their California Air Toxics "Hot Spots" Program, Risk Assessment Guidelines<sup>8</sup>, has proposed for mercury an oral AEL (Acceptable Exposure Level) of 0.3 ug/kg-day, based on the 1991 US EPA HEAST report. The AEL is used for the evaluation of the potential noncancer adverse health effects of long-term (chronic) exposures.

The US EPA<sup>6</sup> has proposed a Maximum Contaminant Level Goal (MCLG) for drinking water of 2 ug/L based on potential adverse kidney effects. This value assumes a drinking water contribution of 20%. The MCLG is similar to the Maximum Contaminant Level (MCL) of 2 ug/L which considers technological and economic feasibility.

The Canadian drinking water objective was set at a maximum acceptable concentration of 1 ug/L.

The above ingestion guidelines are summarized in Table 1.

TABLE 1. Summary of Exposure Guidelines for Mercury from Leading Agencies

GUIDELINE APPLICATION	AGENCY(IES)	ORIGINAL VALUE	CONCENTRATION ("Original Form" converted to these -as applicable)			CALCULATED "ALLOWABLE" INTAKE (3)
			Unit Risk (1)	RsC (2) (1 x 10 <sup>-4</sup> )	RsC (2) (1 x 10 <sup>-4</sup> )	
INHALATION GUIDELINES						
Occupational	ACGIH, OSHA	Alk-Hg: 10 ug/m <sup>3</sup> Hg <sup>2</sup> : 50 ug/m <sup>3</sup> In-Hg: 100 ug/m <sup>3</sup>	NA	NA	NA	200 - 2000 (3 - 30)
Ambient Air Quality Guidelines (similar to chronic AELs/RICs; see below)	Various US states	0.01 - 12 ug/m <sup>3</sup>	NA	NA	NA	0.2 - 240 (0.003 - 3)
Ontario Air Quality Guideline	OMOEE	In-Hg: 2 ug/m <sup>3</sup> Alk-Hg: 0.5 ug/m <sup>3</sup>	NA	NA	NA	In-Hg: 40 (0.6) Alk-Hg: 10 (0.14)
Chronic AELs/RICs	US EPA CAPCOA NYSDEC	Hg <sup>2</sup> : 0.3 ug/m <sup>3</sup> Tot-Hg: 0.3 ug/m <sup>3</sup> In-Hg: 0.3 ug/m <sup>3</sup> Me-Hg: 0.02 ug/m <sup>3</sup>	NA	NA	NA	Hg <sup>2</sup> , Tot-Hg, In-Hg: 6 (0.09) Me-Hg: 0.4 (5.7 x 10 <sup>-3</sup> )
INGESTION GUIDELINES						
Drinking Water Guideline	US EPA MCL Canadian MAC	2 ug/L 1 ug/L	NA	NA	NA	1.5 - 3 (0.02 - 0.04)
AELs/RIDs	US EPA CAPCOA	In-Hg, Me-Hg: 0.3 ug/kg-day	NA	NA	NA	21 (0.3)

<sup>1</sup>For inhalation and ingestion guidelines, unit risks are expressed as (ug/m<sup>3</sup>)<sup>-1</sup> and (ug/L)<sup>-1</sup>, respectively<sup>2</sup>For inhalation and ingestion guidelines, risk specific concentrations are expressed as ug/m<sup>3</sup> and ug/L, respectively<sup>3</sup>Intake was computed by assuming, where applicable, an adult weight of 70 kg, a breathing rate of 20 m<sup>3</sup>/day, a water intake of 1.5 L/day. In all cases 100% bioavailability of the intake was assumed.

### 3. HUMAN EXPOSURE ASSESSMENT

#### 3.1 Inhalation

##### 3.1.1 Ambient Air Quality

Ambient levels of gaseous inorganic mercury (ie. mostly elemental mercury and some  $\text{HgCl}_2$  and  $\text{HgO}$ ) have been measured at nineteen sites in Windsor, over a period of eight days in 1992<sup>16</sup>. Measurements were taken by the Ontario Ministry of the Environment's mobile monitoring group. A total of fifty-one half-hour average samples were obtained and peak samples (ie. highest of the six 5-minute averages during the half-hour period). In this assessment, for each of the nineteen sites the average of the half-hour averages (ie. to give a representative 'mean' for each site) and the average of the peak samples (ie. to give a representative 'maximum' for each site) were calculated. The range of the 'means' were between 1.3 and 52  $\text{ng}/\text{m}^3$ , and the range of the maxima were between 1.6 and 94  $\text{ng}/\text{m}^3$ . It should be noted that with the exception of the site having the 52  $\text{ng}/\text{m}^3$  mean value, all other means were less than 8  $\text{ng}/\text{m}^3$ . Similarly for the maxima, with the exception of the site having a maximum of 94  $\text{ng}/\text{m}^3$ , all other maxima were less than 16  $\text{ng}/\text{m}^3$ . Therefore, the mean value of 8  $\text{ng}/\text{m}^3$  and a maximum value of 16  $\text{ng}/\text{m}^3$  were selected as representative values for the whole urban area. Since this short-term data was the only monitoring information available, it was also assumed that these values are representative over a longer period (ie. the duration of the study).

It is possible to estimate the daily intake of mercury associated with these measures of Windsor ambient air quality, recognizing that personal real exposures/intakes may be quite different as further discussed in section 3.1.2. Table 2 below shows these estimated intakes for two different receptors, i.e., an adult and a child. It should be noted that these intakes were calculated based on 24 hour exposures and assume 100% bioavailability by the inhalation route.

##### 3.1.2 Microenvironments

It is reasonable to assume that the daily mercury intakes associated with typical personal exposure patterns will be different from those based on the above cited monitoring data. With most of the substances on the Windsor focus list, this evaluation was based on various microenvironmental concentrations. For the purpose of scoping population exposures, the set of typical receptors in Table 3

Table 2. Estimated Daily Intakes of Mercury (ie. gaseous inorganic mercury) Associated With Ambient Air Quality in Windsor

Air Quality Measure(a)	Concentration $\text{ng}/\text{m}^3$	Adult(b) $\mu\text{g}/\text{day}$ ( $\mu\text{g}/\text{kg}\cdot\text{day}$ )	Child(b) $\mu\text{g}/\text{day}$ ( $\mu\text{g}/\text{kg}\cdot\text{day}$ )
Mean	8	0.2 (0.003)	0.04 (0.003)
Maximum	16	0.3 (0.004)	0.08 (0.005)
a) Based on 51, half-hour average samples from 19 sites in Windsor b) Assuming the following weights and inhalation rates per day (ie. per 24 hour period): Adult: 70 kg; 20 $\text{m}^3/\text{day}$ Child: 15 kg; 5 $\text{m}^3/\text{day}$			

below was normally considered. Examples of the receptor types and/or their characteristics are also included in Table 3. For mercury, Windsor-specific microenvironment and personal exposure concentrations were not available. Furthermore indoor concentrations of mercury from other studies, that would be deemed to be representative of 'typical personal exposure' patterns were not available. In the one study (p. 125, in Reference 1) that was found, levels of mercury averaged 920 ng/m<sup>3</sup>, in the 'home air' of workers, who worked at a chlor-alkali plant in Tennessee. This was not deemed to be a representative situation and was not used in this evaluation.

**Table 3. Receptors With Typical Personal Exposure Patterns**

NAME OF RECEPTOR TYPE	CHARACTERISTICS	NAME OF RECEPTOR TYPE	CHARACTERISTICS
Average Office Worker (Non-smoking)	Eg. - Typical office worker (Based on Windsor volunteers and US EPA TEAM study; not smoking at home)	High Outdoor Receptor	Eg. - Construction workers; - Bicycle couriers - Police - Long distance runners
Average Office Worker (Smoker Environment)	Eg. - Typical office worker (Based on Windsor volunteers and US EPA TEAM study; smoking at home)	High Indoor Receptor	Eg. - 'Shut-ins'- Invalids - Elderly, non-mobile
Average Youth	Eg. Special exposures at shopping malls and athletic facilities (pools) in addition to school;	High Commuting Receptor	Eg. - Bus drivers - Taxi drivers - Delivery/ Distribution Services
Average Child (Non-Smoker Home & No Exposure to Tobacco Smoke)	Eg. Similar to average office worker except 'School' replaces 'Office';	Active Receptor # 1	Eg.- 7 hr/week in Bingo Hall or Bar
Average Child (Non-Smoker Home & Typical Exposure to Tobacco Smoke)	Eg. Includes typical times that children may be in proximity to tobacco smoke, outside the home, based on activity pattern studies;		
Average Child (Smoker Home with Exposure to Tobacco Smoke)	Eg. Child living in a house where there is a smoker		

In order to place the inhalation exposures (ie. intakes) in Windsor in perspective, it is appropriate to compare to daily intakes that people who smoke or who have dental amalgams may experience.

### 3.1.3 Smoking.

No data was available regarding contribution of mercury from smoking.



### 3.1.4 Dental amalgams.

According to WHO (Reference 17; p.40), *dental amalgams account for the major background intake of mercury vapour*. The estimated intake of inorganic mercury vapour is 3.8 - 21 ug/day. The possibility exists that some of the vapour may dissolve in the saliva as inorganic mercury, but there is no firm evidence for this. A recent study (Skare *et. al.*)<sup>18</sup> of mercury intake by dentists and dental nurses suggests that the contribution from their own amalgams is about 10 ug/day. This was calculated as follows: the excretion in urine was about 2 ug/day. Since ≈80% of the inhaled vapour is retained in the body (Ref. 1, p.52), the amount excreted is the remaining 20% and thus the intake is (2/0.2) or 10 ug/day.

It is also important to place the inhalation exposures (ie. intakes) in Windsor into perspective, relative to general exposures from other media (ie. see section 3.2).

## 3.2 Other Routes

In this section, possible non-inhalation routes of exposure (ie. ingestion and dermal) are estimated.

### 3.2.1 Ingestion of Food

The US-FDA total diet study (1982-84) estimated that the average daily intake of total mercury is 0.49 ug/day for infants and 3.9 ug/day for males in the 25-30 yr age group. The intake for women in the same age bracket was 2.9 ug/day. WHO (Reference 17; p.37) cites the following figures for a 1984-86 FDA market basket study:

Infants:	0.32 ug/day
14-16 yr, female:	1.76
male:	1.84
25-30 yr, female:	2.32
male:	3.01
60-65 yr, female:	2.29
male:	2.52

Expressed on a body weight basis, the intake for all age groups except 2-year old children was approximately 50 ng/kg-day. For the children, the intake was approximately 100 ng/kg-day. The intakes were calculated from measured and assumed trace levels in food representative of the "total diet" of the US population. The predominant source in the diet is fish and fish products. Methylmercury makes up >99% of the mercury in fish muscle with no detection of inorganic or other methylated species (Reference 1, ch.5).

The estimates by the World Health Organization (Reference 17, Table 4) of the daily intake of total and methyl mercury in the general population not occupationally exposed to mercury are given in Table 4.

For a 70 kg adult, the total amounts to 61 ng/kg-day of inorganic and 34 ng/kg-day of methylmercury or a total of 95 ng/kg-day, which is about twice the FDA estimate. The WHO assumed that the daily intake of total mercury from fish and fish products was 3 ug/day and that, in contrast to the ATSDR report, 20% was in the inorganic form. The intake from the non-fish sources was obtained by subtracting the fish intake from the total daily intake. The latter figure was based on US and Belgian data only.

The estimated average intake of the Canadian adult population is given in the following table (Reference 12, Table 5.6). According to the report, mercury in fish is generally 60-95% methyl mercury (Reference 12,



p.15). It assumes that, in calculating the intakes, in fish, 20% is inorganic and in other foods, 100% is inorganic. The estimated adult intakes of the various forms of mercury, based on the H&W report<sup>12</sup> is given in Table 4A. No values were available for children.

**TABLE 4 - INGESTION INTAKE OF MERCURY AS ESTIMATED BY THE WORLD HEALTH ORGANIZATION.**

EXPOSURE	ELEMENTAL MERCURY VAPOUR (ug/day)	INORGANIC MERCURY COMPOUNDS (ug/day)	METHYLMERCURY (ug/day)
Food: fish	0	0.60	2.4
non-fish	0	3.6	0
Drinking water	0	0.05	0
TOTAL	0	4.25	2.4

**TABLE 4A - AVERAGE INGESTION INTAKE OF MERCURY FOR THE ADULT CANADIAN POPULATION**

EXPOSURE	ELEMENTAL MERCURY VAPOUR (ug/day)	INORGANIC MERCURY COMPOUNDS (ug/day)	METHYLMERCURY (ug/day)
Food: fish	0	0.3	1.1
non-fish	0	8.0	0
Drinking water	0	0.06	0.02
TOTAL	0	8.4	1.1

For a 70 kg adult, this amounts to 120 ng/kg-day of inorganic and 16 ng/kg-day of methylmercury for a total of 136 ng/kg-day, or about 2.7 times the FDA estimate. It is, however, close to the Belgian data (140 ng/kg-day) cited by WHO (Reference 17, p.39). The reasons for the differences are unclear. The HWC estimates are based on Canadian figures for food intake and Canadian and international figures for mercury concentrations. The FDA estimates are based on a similar methodology (Reference 1, ch.5). A detailed comparison of the food intake and concentration values would be necessary to identify the reasons for the difference.

The average total mercury concentrations as measured by MOEE in fish caught in the Detroit river and western Lake Erie range from 0.11 to 0.16 ug/g. Using the average adult fish consumption of 12 g/day (Reference 12, Table 4.2) gives intakes of 1.3-1.9 ug/day. This is in agreement with the values in the above table.

Metallic mercury is poorly absorbed -  $\approx 0.1\%$  - in the gastro-intestinal tract of humans. About 7% of

divalent mercury is absorbed and about 15% of mercuric nitrate in aqueous solution or bound to calf liver protein is absorbed. About 95% of methylmercury is absorbed (Reference 1, p. 53). Using absorption factors of 0.15 and 0.95 respectively, the uptake from the Canadian diet is  $\leq 20$  ng/kg-day of inorganic and 15 ng/kg-day of methylmercury for a 70 kg adult.

### 3.2.2 Drinking Water

MOEE monitored both the raw and treated water at the Windsor water treatment plant 6 times in 1990. The mean concentration of total mercury in the treated water was 0.025 ug/L, if half the detection limit of 0.02 is assigned to the 4 samples below it. A survey of trace metals in the Great Lakes indicates that the median concentration in Lake Huron is 0.011 ug/L (Rossman and Barres)<sup>19</sup>.

A survey of tap water consumption in Canada was done in 1977/78 by Health and Welfare Canada<sup>20</sup>. The intake covers both tap water drunk directly and tap water based fluids such as coffee, tea, soup etc. The overall Canadian average for the 18 and over age group is 1.49 L/day, with 90% of the group consuming  $< 2.59$  L/day. The mean for children  $< 6$  yr is 0.76 L/day, with 90% of this population consuming  $< 1.5$  L/day.

In the area served by the Windsor water treatment plant, the intakes of total mercury from tap water and tap water based fluids, using 0.02 ug/L as the mean concentration, is:

adults:            0.04-0.06 ug/day

children:        0.02-0.04 ug/day

These intakes are somewhat less than the estimates in Tables 4 and 4A.

### 3.2.3 Soil

Total mercury was measured in soils in the Windsor area in 1990. The surface samples were collected in lawns and parks. The mean concentration for the stations in Windsor itself is 0.08 ug/g dry weight. The range in concentrations is 0.02 - 0.20 ug/g. The concentrations in the rural area around Windsor are lower with a mean of 0.04 ug/g and a range of 0.01 - 0.07 ug/g. It should be noted that 11% of the analyses are below the detection limit of 0.01 ug/g and a further 52% are qualified as being above the detection limit but should be considered as an estimate (Gizyn)<sup>21</sup>.

A reasonable estimate for the amount of ingested soil and dust is 80 mg/day for children and 20 mg/day for adults (Reference 22, Appendix 1), although values as low as 0 for children  $< 1$  yr, 40 mg/day for children 1-6 yr and 10 mg/day for persons  $> 6$  yr have been used (Sheehan *et al*)<sup>23</sup>. Calabrese and Stanek<sup>24</sup> have modelled the relative contributions of soil and indoor dust to the total intake of children. They estimate that about 65% is from outdoor soil or in the range of 10 - 36 mg/day, depending on the trace element used for deriving the ingestion amount. The total intake of dust and soil is in the range of 16 - 55 mg/day. Because of the lack of information on concentrations of mercury in indoor dust, it is assumed that indoor and outdoor concentrations are the same.

The mean amounts of total mercury ingested from soil by adults in Windsor and the rural area, using the mean concentrations and the ingestion amounts (see above), are 1.6 and 0.8 ng/day, respectively, with a

maximum amount of 4 ng/day. The mean amounts ingested by children are 6.4 and 3.2 ng/day, with a maximum amount of 16 ng/day.

There is no information on the bioavailability or speciation of the mercury in the Windsor area soils. The mercuric mercury forms various complexes with chloride and hydroxide ions in soils, depending on pH, salt content and composition of the soil solution. Organic mercurials may be formed through bacteriological activity (Reference 1, p.122).

### 3.2.4 Dermal

#### 3.2.4.1 During Showering and Bathing

US-EPA<sup>10</sup> has developed models for the dermal absorption of both inorganics and organics. The former assumes a steady-state; the latter allows for a transient state.

The equation for the dermal absorption of inorganics is

$$DA_{\text{event}} = K_p C_w t_{\text{event}}$$

where:  $DA_{\text{event}}$  is the dose absorbed per unit area per event  
(mg/cm<sup>2</sup>\*event)

$K_p$  is the permeability constant from water (cm/hr)

$C_w$  is the concentration of a chemical in water (mg/cm<sup>3</sup>)

$t_{\text{event}}$  is the duration of the event (hr/event)

$K_p$  for mercury in water is, depending on the compound,  $1 - 3 \times 10^{-3}$  cm/hr (Reference 10, Table 5-3). The discussion on p.5-84<sup>10</sup> suggests that there is considerable uncertainty attached to these values. The median surface area of a child is 0.731 m<sup>2</sup> (Reference 10, Table 8-4 for ages 4<5 years) and the 90th percentile is 0.821 m<sup>2</sup>. For an adult, the values are, respectively, 1.94 and 2.28 m<sup>2</sup> (Reference 10, Table 8-3). These areas are estimated from models and not measured directly.

The mean concentration in water at Windsor is 0.025 ug/L or  $2.5 \times 10^{-8}$  mg/cm<sup>3</sup>. A shower is assumed to take 0.25 hr; a bath, 0.5 hr. The whole body is assumed to be wet for the duration of the once-daily event.

The amounts absorbed during a shower are then, using the mean, median and 90th percentile values from above and a  $K_p$  for mercury in water of  $2 \times 10^{-3}$  cm/hr:

adult:  $2.4-2.9 \cdot 10^{-4}$  ug/day

child:  $0.9-1.0 \cdot 10^{-4}$  ug/day

The amounts absorbed during a bath are twice the above values.

#### 3.2.4.2 Contact With Soil and Dirt

US-EPA<sup>10</sup> and ATSDR<sup>1</sup> have no information on the dermal absorption of mercury compounds from soil. US-EPA<sup>10</sup> suggests that 0.1 - 1% of the loading of mercury in soil is absorbed over a 24 hr period (Reference 10, p.6-27).

#### 3.2.4.3 From Mercury Vapour in the Air

US-EPA<sup>10</sup> has no information on the dermal absorption of mercury compounds from soil. ATSDR<sup>1</sup> reports that 0.024 ng of total mercury is absorbed per cm<sup>2</sup> of skin for every minute and for every ng of mercury per cm<sup>3</sup> of air. This rate is based on a single report of experiments.

Using this rate and body surface areas of 1.94 and 0.731 m<sup>2</sup> (see s.3.2.4.1), then for an average concentration of 10 ng/m<sup>3</sup> or 10·10<sup>-6</sup> ng/cm<sup>3</sup>, the amount absorbed in 24 hr by an adult is ≈7 ng and by a child is ≈2.5 ng.

### 4. RISK CHARACTERIZATION AND PERSPECTIVES

Exposures, expressed as daily intakes in units of ug/day, were assessed in section 3. Inhalation, ingestion and dermal routes of exposure were considered. Table 5 below summarizes the daily intakes (or ranges of daily intakes) of total mercury, for adults and children, estimated in section 3. It should be noted that in section 3, the intakes for inhalation and sometimes for ingestion assumed 100% bioavailability. The intake for dermal exposures are amounts absorbed systemically and hence already include bioavailability considerations. Table 5 has two columns for both adults and children. The first set of columns (ie. '100 % Bioav') give the intakes with 100 % bioavailability having been assumed; the second set (ie. "Bioav. Incl."), gives intakes for which bioavailability has been taken into consideration (ie. if information was available as noted in the footnotes). This second set of columns should give a better picture of the relative importance of various exposure routes. As far as comparison to exposure guidelines, the intakes in the first set of columns of Table 5 will be used since the exposure guidelines are also expressed as intakes for which we have assumed 100 % bioavailability.

To characterize risks, the various exposure guidelines discussed in Section 2 are compared to the estimated exposures from inhalation and other routes as discussed in Section 3. Because of the assumptions, uncertainties and ranges of values available from both exposures (see Table 5) and the various exposure guidelines (see Table 1), risk characterization is most appropriately done by comparison of ranges of values.

Table 6 below provides a graphic representation of this comparison of exposures and exposure guidelines based on ug intake/day (ie. 'INTAKE in Micrograms per day' increasing upwards on the vertical scale).

The middle section of Table 6, "Exposures", depicts the exposures calculated in Section 3, expressed as intake/day (ie. ug/day). The exposures depicted are: *Outdoor Air Quality* - the exposure from spending 100 % of the day outdoors; *Typical Outdoor Exposure* - the exposure from three hours only outdoors, provided for perspective on the contribution to risk solely from contaminants present in outdoor air; *Typical Personal Exposures* - the range of exposures associated with 'personal activity patterns' (ie. this was not addressed since no data was available from Windsor and appropriate surrogate values were not found). Exposure scenarios are included for adults and children, assuming 20 and 5 m<sup>3</sup>/day inhalation rates respectively. For 'outdoor air quality' (ie. 100% outdoor exposure) and for 'typical outdoor exposures' (ie. 3 hr) the ranges shown, bracket the lowest mean to the highest 90th percentile. The 'personal activity patterns' area is blank since no data was available. For perspective purposes, the exposures attributed to dental amalgams is also depicted in this section.



The left section of Table 6, "Exposure Guidelines", expresses the various guidelines discussed in Section 2 in terms of calculated "allowable" intake/day for adults and children. The values are taken from Table 1. Within each type of guideline group (eg. outdoor air) ranges of exposure guidelines, when available, are indicated. Thus, ranges of Air Quality Guidelines (ie. 'Outdoor Air'), Occupational guidelines (ie. 'Workplace Air'), and ranges of chronic health effects based reference concentrations (ie. 'Chronic RfC/AEL') are shown. The existing MOEE guideline for mercury is also shown as a horizontal bar. Comparison of "Exposure Guidelines" to "Exposures" should be done with care. For example, occupational guidelines are included for perspective purposes only. For caveats regarding this comparison see section 4.1.1 of the main report.

Based on the tabular analysis (Table 5) and the graphic risk characterization (Table 6), the following observations and deductions can be made:

#### **Health messages:**

1) It is apparent that the ingestion route dominates all other exposure routes for mercury (ie. except for people with dental amalgams - see point # 6). The inhalation route appears to be next in importance followed by the dermal route.

2) Table 6 also indicates that all the inhalation exposures are less than the chronic acceptable exposure levels/reference concentrations (ie. 6 ug/day for metallic or total or inorganic mercury in Table 1; "Chronic RfC/AEL" in Table 6) proposed by US EPA, CAPCOA, and NYSDEC. These RfC/AEL values are considered to be purely health based. Therefore, the possibility of long-term health effects is unlikely.

This comparison of exposures to chronic acceptable exposure levels can also be expressed more quantitatively in the form of a hazard index. These hazard index comparisons for all substances are summarized and are found in section 4.1.5 of the main report.

3) According to the WHO, dental amalgams account for the major background intake of mercury vapour. Table 5 and Table 6 indicates that the exposure 'contribution from dental amalgams' exceeds all other inhalation routes of exposure and even exceeds the ingestion route.

4) Total ingestion exposures for adults (ie. 9.6 ug/day in Table 5) are below the AEL/RfD ingestion guidelines (ie. 21 ug/day in Table 1; not shown in Table 6) of US EPA and CAPCOA. Therefore, the possibility of chronic health effects from these ingestion exposures is unlikely.

#### **Regulatory compliance messages:**

5) The risk characterization in Table 6 indicates that, for all the inhalation receptor exposures considered:

- The exposures potentially associated with outdoor air quality (ie. 100 % outdoor exposure assumed), for adults, youth and children, fall in the lower 0.1 % range of the air quality guidelines of various jurisdictions.
- Exposures associated with typical outdoor exposures (ie. ≈3 hr), fall below the range of air quality guidelines (ie. 'outdoor air') of various jurisdictions.

It should be noted that these air quality guidelines may be of different types. Some are purely health based and some are regulatory and therefore may have been influenced by various risk management considerations. The regulatory guidelines may also have different uses (eg. judging the acceptability of air quality per se or judging the incremental addition by a source to the existing air quality).



Table 5. Summary of Estimated Daily Intakes and/or Range of Intakes (in ug /day), from Various Exposure Pathways (ie. intakes, assuming 100 % bioavailability and intakes with bioavailability taken into consideration)

EXPOSURE PATHWAY		ADULT ug/day  (100 % Bioav.)	ADULT ug/day  (Bioav. Incl.)	CHILD ug/day  (100 % Bioav.)	CHILD ug/day  (Bioav. Incl.)
INHALATION	Outdoor Air Quality - Windsor (ie. 100 % outdoor exposure)(a)	0.2 - 0.3	0.2 - 0.3 (d)	0.04 - 0.08	0.04 - 0.08 (d)
	Typical outdoor exposure (ie. = 3hr)(b)	0.03 - 0.04	0.03 - 0.04 (d)	0.005 - 0.01	0.005 - 0.01 (d)
	Typical personal exposures (c)	-		-	
	Smoking(c)	-		-	
	People with dental amalgams (e)	3.8 - 21	3.8 - 21 (d)		
INGESTION	Food (f)	9.5	2.3 (g)		
	Drinking water (h)	0.06	0.02 (g)	0.04	0.01(g)
	Soil (i)	0.002		0.006	
	TOTAL (Ingestion)	9.6	2.3	0.05	0.01
DERMAL	During showering/ bathing	-	0.0003	-	0.0001
	Contact with soil & dirt (i)				
	From mercury vapour in the air	-	0.007	-	0.003
	TOTAL (Dermal)		0.007		0.003

a.) Range of intakes is associated with the range of the 'mean' to '90th percentile'(ie. in this case 'maximum', since 90th percentiles were not available) concentrations in outdoor air. It is to be noted that people are not exposed 24 hours to outdoor air. This estimation assumes 100 % exposure to outdoor air and is a measure of outdoor air quality per se and not of actual exposure.

b.) Range of intakes calculated from the 'mean' to '90th percentile'(ie. in this case 'maximum', since 90th percentiles were not available) concentrations in outdoor air and assuming a 'typical' outdoor air exposure of = 3 hr(ie. corresponding to breathing 2.5 m<sup>3</sup>/3hr for adults and 0.63 m<sup>3</sup>/3hr for children.

c.) No data was available.

d.) 100 % of metallic mercury vapour, the predominant form in the atmosphere, is absorbed across the alveolar membranes(see s. 1.1).

e.) It is believed that the mercury released from the amalgams is in the form of metallic mercury vapour (see s. 3.1.4)

f.) Data taken from Table 4A.

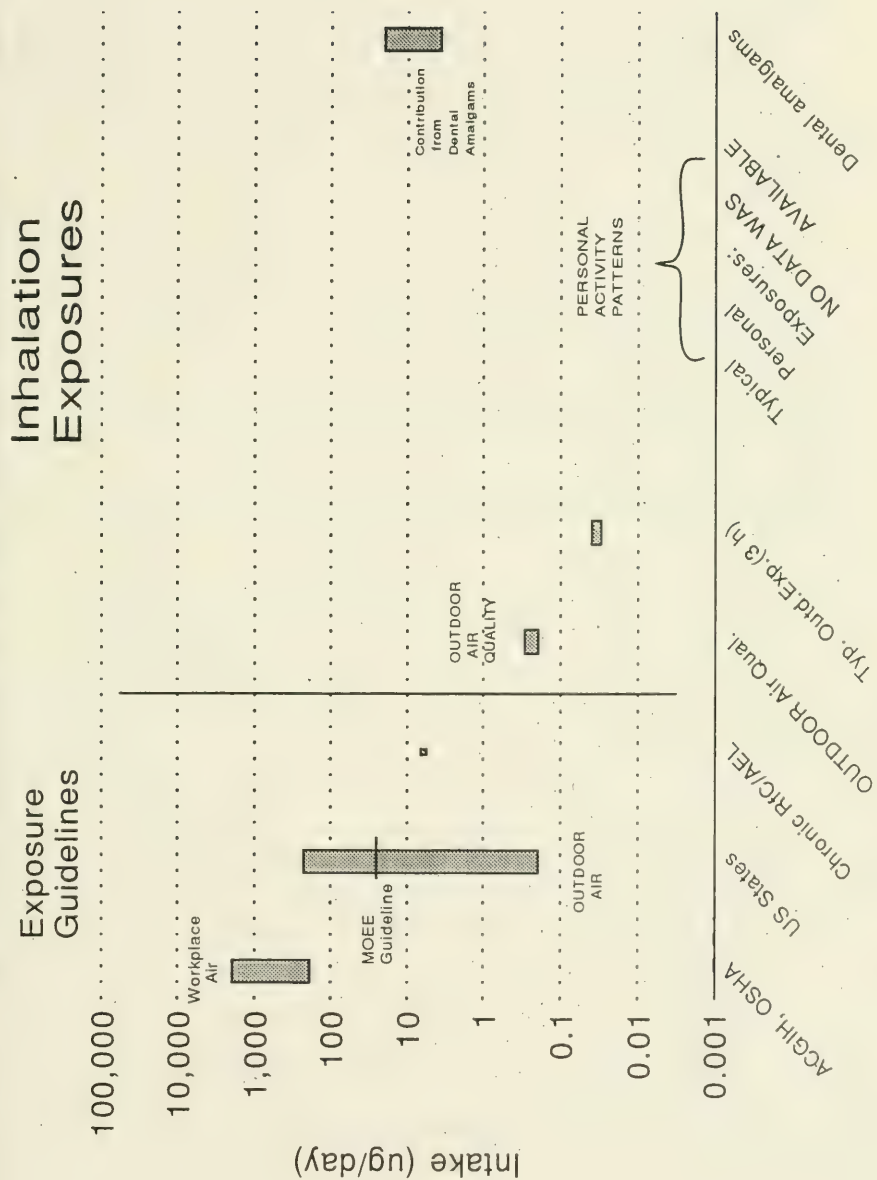
g.) About 15% of the inorganic mercury compounds and 95% of the methylmercury is absorbed (see s. 1.1)

h.) It is assumed that the mercury content is 3/4 inorganic mercury compounds and 1/4 is methylmercury (ie. based on Table 4A and Windsor specific drinking water as in s. 3.2.2)

i.) No information on dermal absorption or absorption via the gastrointestinal tract of mercury in soil is available.

Table 6. MERCURY RISK CHARACTERIZATION in WINDSOR  
Ranges of exposure guidelines and exposures

154000



- 6) All the inhalation exposures are below the existing MOEE guideline (ie. 40 ug/day for inorganic mercury).
- 7) Table 6 also indicates that all the inhalation exposures are less than the range of occupational levels.
- 8) Drinking water exposures (ie. 0.06 ug/day in Table 5) are below the drinking water guidelines of Canada and the US EPA (ie. 1.5 - 3 ug/day in Table 1; not shown in Table 6).
- 9) MOEE is presently reviewing the basis of the existing standards for mercury.

#### Summary and recommendations:

- ♦ All the inhalation exposures are less than the chronic acceptable exposure levels and reference concentrations. These RfC/AEL values are considered to be purely health based. Therefore, the possibility of long-term health effects is unlikely.
- ♦ According to the WHO, dental amalgams account for the major background intake of mercury vapour. The exposure 'contribution from dental amalgams' exceeds all other inhalation routes of exposure and even exceeds the ingestion route.
- ♦ Total ingestion exposures for adults are below the AEL/RfD ingestion guidelines. Therefore, the possibility of chronic health effects from these ingestion exposures is unlikely.

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**APPENDIX 11**

**RISK ANALYSIS FOR PERCHLOROETHYLENE**



## PERCHLOROETHYLENE

### NATURE of the CHEMICAL, SOURCES, LEVELS in OUTDOOR and INDOOR AIR, and ESTIMATED INTAKES.

Perchloroethylene (ie. PCE, Tetrachloroethylene) is a nonflammable, volatile liquid. It is widely used as a dry cleaning agent, and is also extensively used as a solvent in metal degreasing in a variety of industries, such as metal and machine shops and automotive repair shops. There are no known natural sources of PCE. Its main route of entry into the environment is from evaporation during dry cleaning and degreasing uses. Because of this, ambient air concentrations are generally higher in urban areas than rural.

Average (ie. 'mean') and 90th percentile concentrations (or range of concentrations) of perchloroethylene in outdoor and indoor air are summarized in Table 1. Estimated adult intakes per day in units of ug/day, associated with these concentrations, are also included in Table 1.

**Table 1. Levels of Perchloroethylene in Outdoor and Indoor Air in Windsor and, Estimated Intakes per day (in ug/day) Associated with these Environments.**

ENVIRONMENTS	Concentration Mean or Range of Means  ug/m <sup>3</sup>	Concentration 90th percentile (or Range of)  ug/m <sup>3</sup>	Estimated Adult Range of Intakes per day  ug/day
Outdoor Air Quality - Windsor (ie. 100 % outdoor exposure) (a)	0.86	2.01	17.2 - 40.2 (a),(d)
Typical outdoor exposure (ie. ≈ 3hr) (b)	0.86	2.01	2.2 - 5.0 (b)
INDOOR AIR ENVIRONMENTS (c) (EXTENDED periods of exposure expected) (e.g. Home, office)	2.3 - 12.5	5.3 - 13.6	40.3 - 238 (e)
INDOOR AIR ENVIRONMENTS (c) (BRIEF periods of exposure expected) (e.g. Commuting, bingo halls, taverns)	2.5 - 7.6 (g)	8.5 - 15.9	Not included (f)
<p>a) Based on 224, 24 hour average samples. Range of intakes is associated with the range of the 'mean' to '90th percentile' concentrations in outdoor air. It is to be noted that people are not exposed 24 hours to outdoor air. This estimation assumes 100 % exposure to outdoor air and is a measure of outdoor air quality per se and not of actual exposure.</p> <p>b) Range of intakes calculated from the 'mean' to '90th percentile' concentrations in outdoor air and assuming a 'typical' outdoor air exposure of ≈ 3 hr (ie. corresponding to breathing 2.5 m<sup>3</sup>/3hr for adults).</p> <p>c) From the Windsor personal exposure &amp; microenvironment studies</p> <p>d) Assuming an inhalation rate of 20 m<sup>3</sup>/day</p> <p>e) Range of intakes is estimated from the range of the lowest 'mean' and the highest '90th percentile' concentrations obtained from personal exposure and microenvironment measurements in indoor environments in environments where extended periods of exposure are expected. A total exposure of 21 hours (ie. 17.5 m<sup>3</sup>/day) was assumed for these indoor environments.</p> <p>f) Direct estimation of daily intake is not appropriate since relatively small amounts of time is spent in these microenvironments</p> <p>g) Median value was used for the upper end of the range.</p>			

## HEALTH CONCERNS

Both short-term and long-term exposures to levels above 9 ppm (ie.  $>60,000 \text{ ug/m}^3$ ) have been associated with toxic effects in both animals and humans. These effects include dizziness, headache, liver and kidney toxicity and effects on the central nervous system (eg. muscle incoordination)<sup>1</sup>. However, these levels are much higher than any of the highest environmental levels of PCE ever recorded<sup>1</sup>.

The cancer causing potential of PCE has been examined in several animal studies. It has been shown to cause leukemia in rats and liver tumors in mice. U.S. EPA ranks PCE as probable human carcinogen. EPA's Science Advisory Board disputes this and ranks PCE as a possible human carcinogen, a lesser classification.

Various health criteria (ie. Unit risks, Reference concentrations, ambient air quality guidelines) from lead agencies are summarized in Table 2. The table also includes the calculated "allowable" intake associated with the listed health criteria.

## RISK CHARACTERIZATION AND PERSPECTIVES

From the brief exposure analysis and the available health criteria the following observations can be made:

### Health messages:

1) All exposures are less than the range of chronic acceptable exposure levels (ie. 700 - 100000 ug/day) proposed by California (CDHS) and the WHO.

2) The most conservative exposure guidelines available are the potencies shown in Table 3. The carcinogenic risk associated with 'outdoor air quality' (ie. 100 % outdoor exposure) is between  $5.3 \times 10^{-6}$  and  $1.2 \times 10^{-5}$ . Similarly the risk associated with 'typical outdoor exposures' (ie. 3 hr) is between  $6.5 \times 10^{-7}$  and  $1.5 \times 10^{-6}$ . Similarly the range of risks associated with indoor air environments (ie. those in which extended periods of exposure are expected) is between  $1.2 \times 10^{-5}$  and  $7.1 \times 10^{-5}$ . The risks associated with indoor air environments (ie. those in which extended periods of exposure are expected) are slightly higher than the risks associated with 'outdoor air quality' which in turn is higher than 'typical outdoor exposures'. It should be noted that this risk characterization (ie. using carcinogenic based limits) is based on an assumed lifetime exposure (ie. 24 hours, every day, for 70 years) and hence is a very conservative assumption.

3) Exposures associated with indoor environments (ie. those in which extended periods of exposure are expected) exceed those associated with typical outdoor air exposures (ie. 3 hr).

### Regulatory compliance messages:

4) All exposures associated with outdoor air quality (ie. 100 % outdoor exposure) and typical outdoor exposure (ie. 3 hr) fall in the lower 1 % range of air quality guidelines of various jurisdictions. Exposures associated with indoor air environments (ie. those in which extended periods of exposure are expected) fall in the lower 10 % range of air quality guidelines of various jurisdictions. All exposures are less than the Ontario guideline.

5) All exposures are less than the range of occupational levels.

6) MOEE will be reviewing the basis of the existing standard for perchloroethylene.

TABLE 2. Summary of Exposure Guidelines for Perchloroethylene from Leading Agencies

GUIDELINE APPLICATION	AGENCY(IES)	ORIGINAL VALUE	CONCENTRATION ("Original Form" converted to these -as applicable)			CALCULATED "ALLOWABLE" INTAKE (3)
			Unit Risk (1)	R <sub>s</sub> C (2) (1 x 10 <sup>-3</sup> )	R <sub>s</sub> C (2) (1 x 10 <sup>-4</sup> )	
INHALATION GUIDELINES						
Occupational	ACGIH, Ontario	340000-339000 ug/m <sup>3</sup>	NA	NA	NA	6780000 - 6800000 (97.1 - 96.9)
Ambient Air Quality Guidelines	US states,	0.08-190 ug/m <sup>3</sup>	NA	NA	NA	1.6 - 3800 (2.3 x 10 <sup>-4</sup> - 0.05)
Ontario Air Quality Guideline		4000 ug/m <sup>3</sup>				80000 (1.10)
Chronic AELs/RfCs	CDHS WHO	35 ug/m <sup>3</sup> 5000 ug/m <sup>3</sup>	NA	NA	NA	700-100000 (0.01-1.43)
Inhalation Cancer Potency Factor	EPA CDHS WHO	See Unit Risk column	Under review 5.9 x 10 <sup>-4</sup> None proposed	1.7	0.17	for 1 x 10 <sup>-4</sup> risk: 34 (4.9 x 10 <sup>-4</sup> ) for 1 x 10 <sup>-5</sup> risk: 3.4 (4.9 x 10 <sup>-5</sup> )

<sup>1</sup>For inhalation guidelines, unit risks are expressed as (ug/m<sup>3</sup>)<sup>-1</sup>

<sup>2</sup>For inhalation guidelines, risk specific concentrations are expressed as ug/m<sup>3</sup>

<sup>3</sup>Intake was computed by assuming, where applicable, an adult weight of 70 kg, a breathing rate of 20 m<sup>3</sup>/day. In all cases 100% bioavailability of the intake was assumed.



Table 3. Range of Inhalation Cancer Risks Associated with Estimated Intakes (ie. for adult exposures only) of Perchloroethylene

RANGE of INHALATION INTAKES			POTENCY (a)		RANGE of RISKS
Environment	Unit ug/day	Unit mg/kg/day	Agency	Unit (mg/kg-d) <sup>1</sup>	
OUTDOOR AIR QUALITY (Windsor)	17.2 - 40.2	$2.5 \times 10^{-4}$ $5.7 \times 10^{-4}$	EPA	N.A.	
			CDHS	$2.1 \times 10^{-2}$ (a)	$5.3 \times 10^{-6}$ - $1.2 \times 10^{-5}$
			WHO	None proposed	
			OVERALL RANGE OF RISKS: $5.3 \times 10^{-6}$ - $1.2 \times 10^{-5}$		
TYPICAL OUTDOOR EXPOSURE (ie.: 3 hr.)	2.2 - 5.0	$3.1 \times 10^{-6}$ $7.1 \times 10^{-6}$	EPA	N.A.	
			CDHS	$2.1 \times 10^{-2}$ (a)	$6.5 \times 10^{-7}$ - $1.5 \times 10^{-6}$
			WHO	None proposed	
			OVERALL RANGE OF RISKS: $6.5 \times 10^{-7}$ - $1.5 \times 10^{-6}$		
INDOOR AIR ENVIRONMENTS (Extended periods of exposure expected)	40.3 - 238	$5.8 \times 10^{-4}$ - $3.4 \times 10^{-3}$	EPA	N.A.	
			CDHS	$2.1 \times 10^{-2}$ (a)	$1.2 \times 10^{-5}$ - $7.1 \times 10^{-5}$
			WHO	None proposed	
			OVERALL RANGE OF RISKS: $1.2 \times 10^{-5}$ - $7.1 \times 10^{-5}$		
a. These are equivalent potency factors calculated from the unit risks proposed by the agencies listed; assumed adult weight of 70 kg and 20 m <sup>3</sup> per day.					

#### Summary and recommendations:

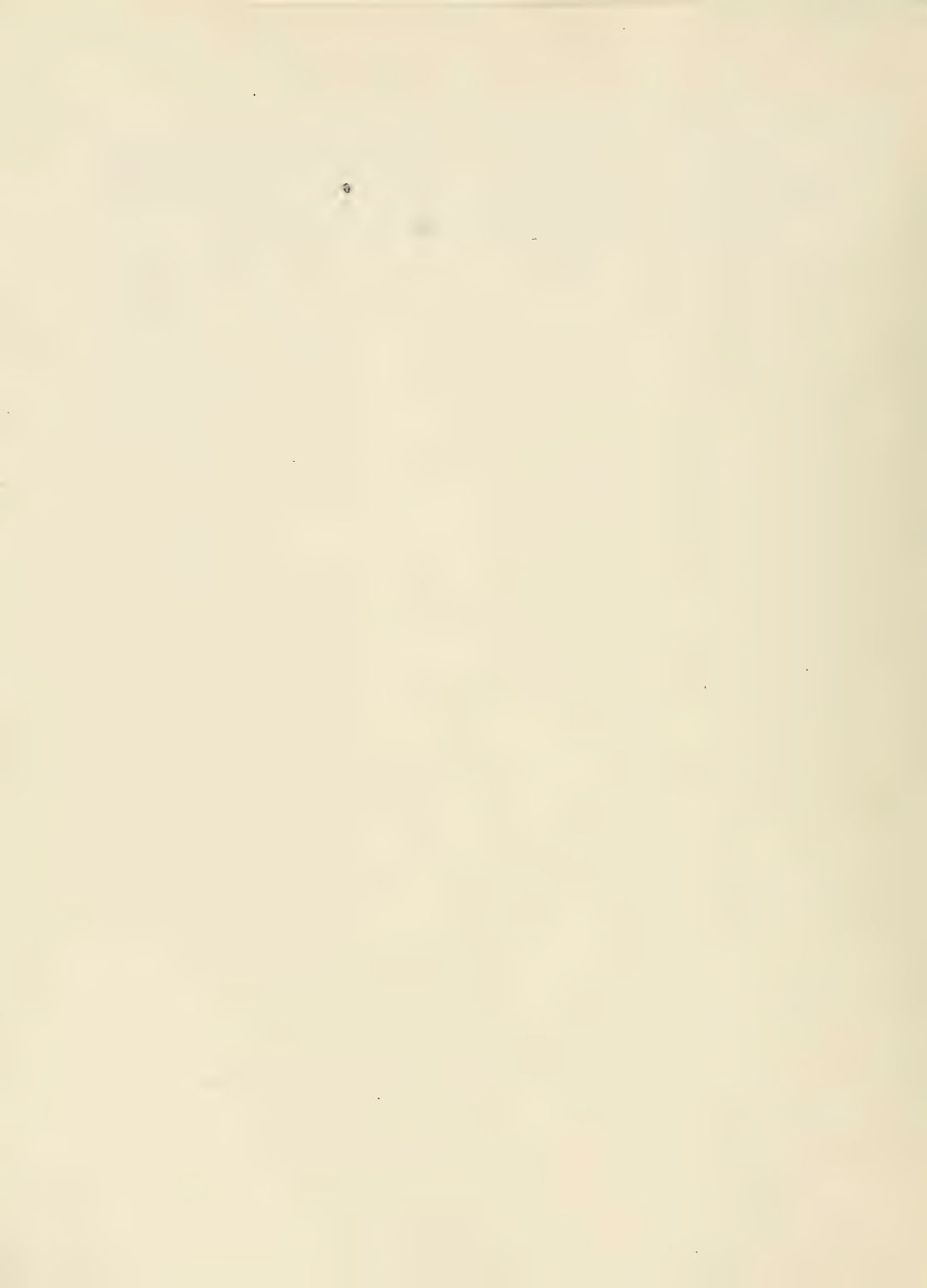
- ♦ All exposures are less than the range of chronic acceptable exposure levels. Therefore, the possibility of long-term health effects, other than cancer risk, is unlikely.
- ♦ Since the levels of inhalation risk exceed  $1 \times 10^{-5}$ , a level generally deemed to be negligible, it is recommended that perchloroethylene be considered a candidate for reduction of exposure.

#### REFERENCES

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## APPENDIX 12

### RISK ANALYSIS FOR METHYLENE CHLORIDE



## METHYLENE CHLORIDE

### NATURE of the CHEMICAL, SOURCES, LEVELS in OUTDOOR and INDOOR AIR, and ESTIMATED INTAKES.

Methylene chloride (ie. dichloromethane) is a nonflammable, volatile liquid. It is widely used as a paint stripper, foam-blowing agent, and as a solvent in aerosol products, metal degreasing compounds in the electronics industry, and in pesticides. There are no known natural sources of methylene chloride. Its main route of entry into the environment is from evaporation during use of paint removers, aerosol spray cans, metal degreasers, fumigants, and foam-blowers. Because of this, ambient air concentrations are generally higher in urban areas than rural.

Average (ie. 'mean') and 90th percentile concentrations (or range of concentrations) of methylene chloride in outdoor and indoor air are summarized in Table 1. Estimated adult intakes per day in units of ug/day, associated with these concentrations, are also included in Table 1.

**Table 1. Levels of Methylene chloride in Outdoor and Indoor Air in Windsor and, Estimated Intakes per day (in ug/day) Associated with these Environments.**

ENVIRONMENTS	Concentration Mean or Range of Means  ug/m <sup>3</sup>	Concentration 90th percentile (or Range of)  ug/m <sup>3</sup>	Estimated Adult Range of Intakes per day  ug/day
Outdoor Air Quality - Windsor (ie. 100 % outdoor exposure) (a)	1.41	2.75	28.2 - 55.0 (a), (d)
Typical outdoor exposure (ie. = 3hr) (b)	1.41	2.75	3.5 - 6.9 (b)
INDOOR AIR ENVIRONMENTS (c) (EXTENDED periods of exposure expected) (e.g. Home, office)	1.7 - 8.6	2.7 - 29.3	29.8 - 513 (e)
INDOOR AIR ENVIRONMENTS (c) (BRIEF periods of exposure expected) (e.g. Commuting, bingo halls, taverns)	2.0 - 3.9	3.3 - 8.5	Not included (f)

a) Based on 201, 24 hour average samples. Range of intakes is associated with the range of the 'mean' to '90th percentile' concentrations in outdoor air. It is to be noted that people are not exposed 24 hours to outdoor air. This estimation assumes 100 % exposure to outdoor air and is a measure of outdoor air quality per se and not of actual exposure.

b) Range of intakes calculated from the 'mean' to '90th percentile' concentrations in outdoor air and assuming a 'typical' outdoor air exposure of ~ 3 hr (ie. corresponding to breathing 2.5 m<sup>3</sup>/hr for adults).

c) From the Windsor personal exposure & microenvironment studies

d) Assuming an inhalation rate of 20 m<sup>3</sup>/day

e) Range of intakes is estimated from the range of the lowest 'mean' and the highest '90th percentile' concentrations obtained from personal exposure and microenvironment measurements in indoor environments in environments where extended periods of exposure are expected. A total exposure of 21 hours (ie. 17.5 m<sup>3</sup>/day) was assumed for these indoor environments.

f) Direct estimation of daily intake is not appropriate since relatively small amounts of time is spent in these microenvironments

## HEALTH CONCERNS

Both short-term and long-term exposures to levels above 25 ppm (ie.  $>88,250 \text{ ug/m}^3$ ) have been associated with toxic effects in both animals and humans. These effects include eye irritation, visual and auditory disturbances, dizziness, nausea, liver and kidney toxicity and effects on the central nervous system<sup>1</sup>. However, these effect levels are much higher than the concentrations of methylene chloride measured in the environment.

The cancer causing potential of methylene chloride has been examined in several animal studies. It has been shown to cause lung and liver tumors in mice and benign mammary gland tumors in rats. U.S. EPA ranks methylene chloride as a probable human carcinogen.

Various health criteria (ie. Unit risks, Reference concentrations, ambient air quality guidelines) from lead agencies are summarized in Table 2. The table also includes the calculated "allowable" intake associated with the listed health criteria.

## RISK CHARACTERIZATION AND PERSPECTIVES

From the brief exposure analysis and the available health criteria the following observations can be made:

### Health messages:

- 1) All exposures are less than the range of chronic acceptable exposure levels (ie.  $60000 \text{ ug/day}$ ) proposed by California (CDHS) and the WHO.
- 2) The most conservative exposure guidelines available are the potencies shown in Table 3. The carcinogenic risk associated with 'outdoor air quality' (ie. 100 % outdoor exposure) is between  $6.8 \times 10^{-7}$  and  $2.8 \times 10^{-6}$ . Similarly the risk associated with 'typical outdoor exposures' (ie. 3 hr) is between  $8.5 \times 10^{-8}$  and  $3.6 \times 10^{-7}$ . Similarly the range of risks associated with indoor air environments (ie. those in which extended periods of exposure are expected) is between  $7.3 \times 10^{-7}$  and  $2.6 \times 10^{-5}$ . The risks associated with indoor air environments (ie. those in which extended periods of exposure are expected) are slightly higher than the risks associated with 'outdoor air quality' which in turn is higher than 'typical outdoor exposures'. It should be noted that this risk characterization (ie. using carcinogenic based limits) is based on an assumed lifetime exposure (ie. 24 hours, every day, for 70 years) and hence is a very conservative assumption.
- 3) Exposures associated with indoor environments (ie. those in which extended periods of exposure are expected) exceed those associated with typical outdoor air exposures (ie. 3 hr).

### Regulatory compliance messages:

- 4) All exposures associated with outdoor air quality (ie. 100 % outdoor exposure) and typical outdoor exposure (ie. 3 hr) fall in the lower 10 % range of air quality guidelines of various jurisdictions. Exposures associated with indoor air environments (ie. those in which extended periods of exposure are expected) fall within the air quality guidelines of various jurisdictions. All exposures are less than the Ontario guideline.
- 5) All exposures are less than the range of occupational levels.
- 6) MOEE will be reviewing the basis of the existing standard for methylene chloride.



TABLE 2. Summary of Exposure Guidelines for Methylene chloride from Leading Agencies

GUIDELINE APPLICATION	AGENCY(IES)	ORIGINAL VALUE	CONCENTRATION ("Original Form" converted to these -as applicable)			CALCULATED "ALLOWABLE" INTAKE (3)
			Unit Risk (1)	R5C (2) (1 x 10 <sup>-3</sup> )	R5C (2) (1 x 10 <sup>-4</sup> )	
INHALATION GUIDELINES						
Occupational	ACGIH, Ontario	174000-175000 ug/m <sup>3</sup>	NA	NA	NA	3480000 - 3500000 (49.7 - 50)
Ambient Air Quality Guidelines	US states,	0.24-27 ug/m <sup>3</sup>	NA	NA	NA	4.8 - 540 (6.8 x 10 <sup>-2</sup> - 7.7 x 10 <sup>-3</sup> )
Air Quality Guideline	Ontario	1765 ug/m <sup>3</sup>	NA	NA	NA	35300 (0.50)
Chronic AELs/RfCs	CDHS WHO	3000 ug/m <sup>3</sup> 3000 ug/m <sup>3</sup>	NA	NA	NA	60000 (0.857)
Inhalation Cancer Potency Factor	EPA CDHS WHO	See Unit Risk column	4.7 x 10 <sup>-7</sup> 1 x 10 <sup>-4</sup> None proposed	20 10	2 1	for 1 x 10 <sup>-4</sup> risk: 200-400 (0.003-0.006) for 1 x 10 <sup>-4</sup> risk: 20-40 (0.003-0.006)

<sup>1</sup>For Inhalation guidelines, unit risks are expressed as (ug/m<sup>3</sup>)<sup>-1</sup>

<sup>2</sup>For Inhalation guidelines, risk specific concentrations are expressed as ug/m<sup>3</sup>

<sup>3</sup>Intake was computed by assuming, where applicable, an adult weight of 70 kg, a breathing rate of 20 m<sup>3</sup>/day. In all cases 100% bioavailability of the intake was assumed.

Table 3. Range of Inhalation Cancer Risks Associated with Estimated Intakes (ie. for adult exposures only) of Methylene chloride

RANGE of INHALATION INTAKES			POTENCY (a)		RANGE of RISKS
Environment	Unit ug/day	Unit mg/kg/day	Agency	Unit (mg/kg-d) <sup>a</sup>	
OUTDOOR AIR QUALITY (Windsor)	28.2 - 55	$4.0 \times 10^{-4}$ $7.9 \times 10^{-4}$	EPA	$1.7 \times 10^{-3}$ (a)	$6.8 \times 10^{-7}$ - $1.3 \times 10^{-6}$
			CDHS	$3.6 \times 10^{-3}$ (a)	$1.4 \times 10^{-6}$ - $2.8 \times 10^{-6}$
			WHO	None proposed	
			OVERALL RANGE OF RISKS: $6.8 \times 10^{-7}$ - $2.8 \times 10^{-6}$		
TYPICAL OUTDOOR EXPOSURE (ie.= 3 hr.)	3.5 - 6.9	$5.0 \times 10^{-5}$ $9.9 \times 10^{-5}$	EPA	$1.7 \times 10^{-3}$ (a)	$8.5 \times 10^{-8}$ - $1.7 \times 10^{-7}$
			CDHS	$3.6 \times 10^{-3}$ (a)	$1.8 \times 10^{-7}$ - $3.6 \times 10^{-7}$
			WHO	None proposed	
			OVERALL RANGE OF RISKS: $8.5 \times 10^{-8}$ - $3.6 \times 10^{-7}$		
INDOOR AIR ENVIRONMENTS (Extended periods of exposure expected)	29.8 - 513	$4.3 \times 10^{-4}$ - $7.3 \times 10^{-3}$	EPA	$1.7 \times 10^{-3}$ (a)	$7.3 \times 10^{-7}$ - $1.2 \times 10^{-6}$
			CDHS	$3.6 \times 10^{-3}$ (a)	$1.6 \times 10^{-6}$ - $2.6 \times 10^{-6}$
			WHO	None proposed	
			OVERALL RANGE OF RISKS: $7.3 \times 10^{-7}$ - $2.6 \times 10^{-6}$		
a. These are equivalent potency factors calculated from the unit risks proposed by the agencies listed; assumed adult weight of 70 kg and 20 m <sup>3</sup> per day.					

#### Summary and recommendations:

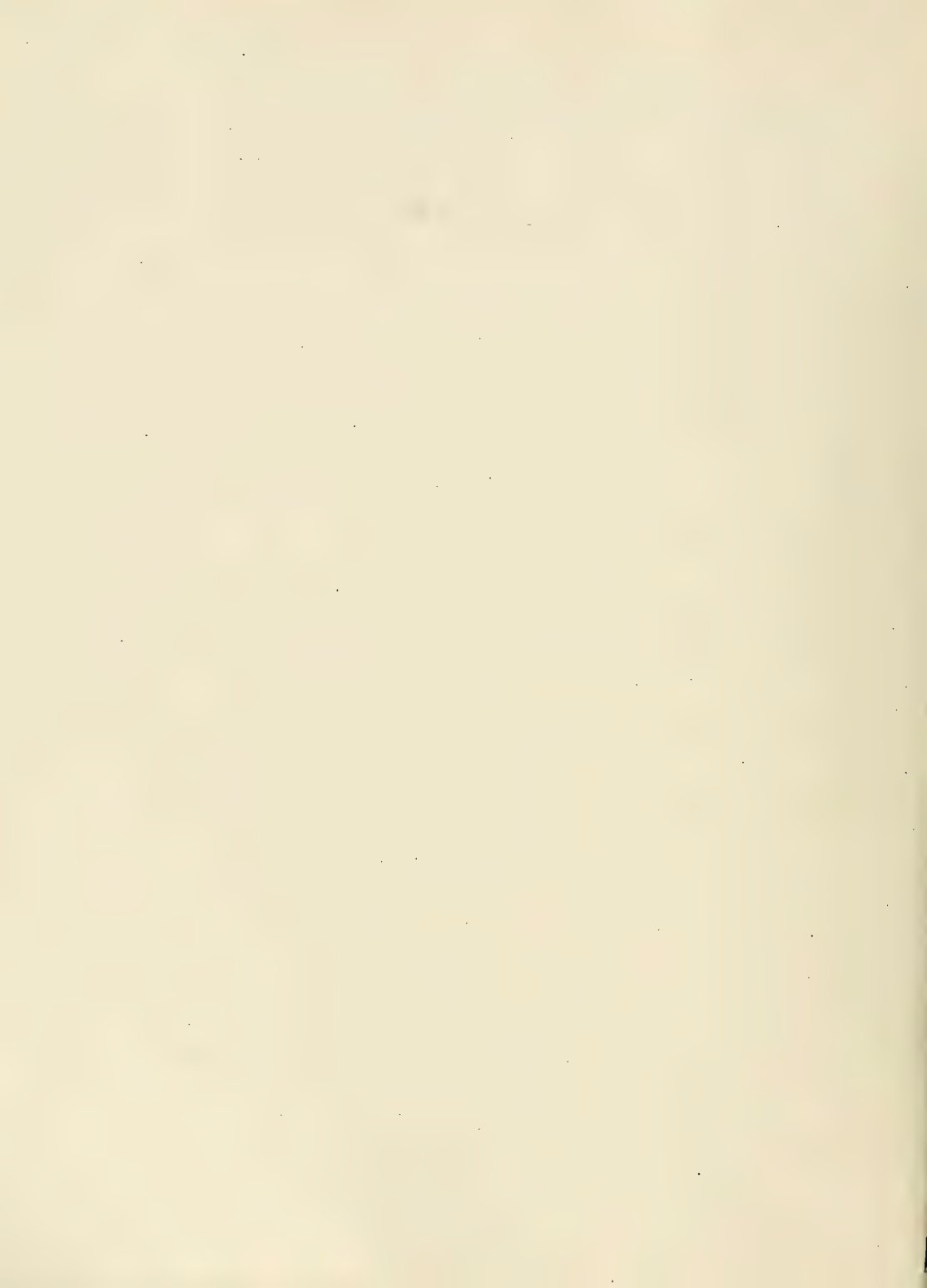
- ♦ All exposures are less than the range of chronic acceptable exposure levels. Therefore, the possibility of long-term health effects, other than cancer risk, is unlikely.
- ♦ Since the levels of inhalation risk are generally below  $1 \times 10^{-5}$  (except in some indoor air environments), a level generally deemed to be negligible, it is not necessary to place a high priority on exposure reduction for methylene chloride.

#### REFERENCES

1. Agency for Toxic Substances and Disease Registry, U.S. Public Health Service. Toxicological Profile for Methylene chloride (Draft). October 1991.

**APPENDIX 13**

**RISK ANALYSIS FOR ETHYLENE DICHLORIDE**



## ETHYLENE DICHLORIDE

### NATURE of the CHEMICAL, SOURCES, LEVELS in OUTDOOR and INDOOR AIR, and ESTIMATED INTAKES.

Ethylene dichloride (1,2-dichloroethane) is a clear, volatile liquid at room temperature and pressure and has a pleasant smell and a sweet taste. It is widely used as a chemical intermediate in the synthesis of, for example, vinyl chloride, as a solvent for grease, glue, and dirt, and finally as a lead scavenger in leaded gasoline. Ethylene dichloride is not formed in nature. Its main route of entry into the environment is from emissions from industries that produce, use, store, or distribute the compound. Because of this, ambient air concentrations are generally higher in urban areas than rural.

Average (ie. 'mean') and 90th percentile concentrations (or range of concentrations) of ethylene dichloride in outdoor and indoor air are summarized in Table 1. Estimated adult intakes per day in units of ug/day, associated with these concentrations, are also included in Table 1.

**Table 1. Levels of Ethylene dichloride in Outdoor and Indoor Air in Windsor and, Estimated Intakes per day (in ug/day) Associated with these Environments.**

ENVIRONMENTS	Concentration Mean or Range of Means  ug/m <sup>3</sup>	Concentration 90th percentile (or Range of)  ug/m <sup>3</sup>	Estimated Adult Range of Intakes per day  ug/day
Outdoor Air Quality - Windsor (ie. 100 % outdoor exposure) (a)	0.07	0.17	1.4 - 3.4 (a),(d)
Typical outdoor exposure (ie. ~ 3hr) (b)	0.07	0.17	0.2 - 0.4 (b)
INDOOR AIR ENVIRONMENTS (c) (EXTENDED periods of exposure expected) (e.g. Home, office)	1.1	1.5	19.3 - 26.3 (e)
INDOOR AIR ENVIRONMENTS (c) (BRIEF periods of exposure expected) (e.g. Commuting, bingo halls, taverns)	1.8	3.9 - 10.4(g)	Not included (f)

a) Based on 224, 24 hour average samples. Range of intakes is associated with the range of the 'mean' to '90th percentile' concentrations in outdoor air. It is to be noted that people are not exposed 24 hours to outdoor air. This estimation assumes 100 % exposure to outdoor air and is a measure of outdoor air quality per se and not of actual exposure.

b) Range of intakes calculated from the 'mean' to '90th percentile' concentrations in outdoor air and assuming a 'typical' outdoor air exposure of ~ 3 hr (ie. corresponding to breathing 2.5 m<sup>3</sup>/3hr for adults).

c) From the Windsor personal exposure & microenvironment studies. The values in the 'mean' and '90th percentile' columns are the minimum and maximum values, respectively, taken from a limited data set.

d) Assuming an inhalation rate of 20 m<sup>3</sup>/day

e) Range of intakes is estimated from the range of the minimum and maximum concentrations obtained from personal exposure and microenvironment measurements in indoor environments in environments where extended periods of exposure are expected. A total exposure of 21 hours (ie. 17.5 m<sup>3</sup>/day) was assumed for these indoor environments.

f) Direct estimation of daily intake is not appropriate since relatively small amounts of time is spent in these microenvironments

g) This is a single maximum value.



## HEALTH CONCERNS

Both short-term and long-term exposures to levels above 2.3 ppm (ie.  $>9292 \text{ ug/m}^3$ ) have been associated with toxic effects in both animals and humans. These effects include central nervous system depression, immune system suppression, and lesions in the heart, liver, and kidneys. However, these effects levels are much higher than the concentrations of ethylene dichloride measured in the environment.

The cancer causing potential of ethylene dichloride has been examined in several animal studies. It has been shown to cause tumors of the stomach, circulatory system and mammary glands in rats; in mice, tumors developed in the lungs, liver, mammary glands and uterus. U.S.EPA ranks ethylene dichloride as a probable human carcinogen.

Various health criteria (ie. Unit risks, Reference concentrations, ambient air quality guidelines) from lead agencies are summarized in Table 2. The table also includes the calculated "allowable" intake associated with the listed health criteria.

## RISK CHARACTERIZATION AND PERSPECTIVES

From the brief exposure analysis and the available health criteria the following observations can be made:

### Health messages:

- 1) All exposures are less than the range of chronic acceptable exposure levels (ie. 1900 - 14000 ug/day) proposed by California (CDHS) and the WHO.
- 2) The most conservative exposure guidelines available are the potencies shown in Table 3. The carcinogenic risk associated with 'outdoor air quality' (ie. 100 % outdoor exposure) is between  $1.4 \times 10^{-6}$  and  $4.5 \times 10^{-6}$ . Similarly the risk associated with 'typical outdoor exposures' (ie. 3 hr) is between  $2.0 \times 10^{-7}$  and  $5.2 \times 10^{-7}$ . Similarly the range of risks associated with indoor air environments (ie. those in which extended periods of exposure are expected) is between  $2.0 \times 10^{-5}$  and  $3.5 \times 10^{-5}$ . The risks associated with indoor air environments (ie. those in which extended periods of exposure are expected) are slightly higher than the risks associated with 'outdoor air quality' which in turn is higher than 'typical outdoor exposures'. It should be noted that this risk characterization (ie. using carcinogenic based limits) is based on an assumed lifetime exposure (ie. 24 hours, every day, for 70 years) and hence is a very conservative assumption.
- 3) Exposures associated with indoor environments (ie. those in which extended periods of exposure are expected) exceed those associated with typical outdoor air exposures (ie. 3 hr).

### Regulatory compliance messages:

- 4) All exposures associated with outdoor air quality (ie. 100 % outdoor exposure) and typical outdoor exposure (ie. 3 hr) fall in the lower 5 % range of air quality guidelines of various jurisdictions. Exposures associated with indoor air environments (ie. those in which extended periods of exposure are expected) fall in the lower 35 % range of air quality guidelines of various jurisdictions. All exposures are less than the Ontario guideline.
- 5) All exposures are less than the range of occupational levels.
- 6) MOEE will be reviewing the basis of the existing standard for ethylene dichloride.

TABLE 2. Summary of Exposure Guidelines for Ethylene dichloride from Leading Agencies

GUIDELINE APPLICATION	AGENCY(IES)	ORIGINAL VALUE	CONCENTRATION ("Original Form" converted to these -as applicable)			CALCULATED "ALLOWABLE" INTAKE (3)
			Unit Risk (1)	R <sub>50</sub> (2) (1 x 10 <sup>-3</sup> )	R <sub>50</sub> (2) (1 x 10 <sup>-4</sup> )	
INHALATION GUIDELINES						
Occupational	ACGIH, Ontario	40000 ug/m <sup>3</sup>	NA	NA	NA	800000 (11.4)
Ambient Air Quality Guidelines	US states,	0.04-4 ug/m <sup>3</sup>	NA	NA	NA	0.8-80 (1.1 x 10 <sup>-5</sup> - 1.1 x 10 <sup>-3</sup> )
Air Quality Guideline	Ontario	400 ug/m <sup>3</sup>	NA	NA	NA	8000 (0.1)
Chronic AELs/RfCs	CDHS WHO	95 ug/m <sup>3</sup> 700 ug/m <sup>3</sup>	NA	NA	NA	1900-14000 (0.03 - 0.2)
Inhalation Cancer Potency Factor	EPA CDHS WHO	See Unit Risk column	2.6 x 10 <sup>-6</sup> 2 x 10 <sup>-6</sup> None proposed	0.4 0.5 NA	0.04 0.05 NA	for 1 x 10 <sup>-6</sup> risk: 8 - 10 (1.1 x 10 <sup>-4</sup> - 1.4 x 10 <sup>-4</sup> ) for 1 x 10 <sup>-5</sup> risk: 0.8 - 1 (1.1 x 10 <sup>-6</sup> - 1.4 x 10 <sup>-5</sup> )

<sup>1</sup>For inhalation guidelines, unit risks are expressed as (ug/m<sup>3</sup>)<sup>-1</sup>

<sup>2</sup>For inhalation guidelines, risk specific concentrations are expressed as ug/m<sup>3</sup>

<sup>3</sup>Intake was computed by assuming, where applicable, an adult weight of 70 kg, a breathing rate of 20 m<sup>3</sup>/day. In all cases 100% bioavailability of the intake was assumed.

Table 3. Range of Inhalation Cancer Risks Associated with Estimated Intakes (ie. for adult exposures only) of Ethylene dichloride.

RANGE of INHALATION INTAKES			POTENCY (a)		RANGE of RISKS
Environment	Unit ug/day	Unit mg/kg/day	Agency	Unit (mg/kg-d) <sup>1</sup>	
OUTDOOR AIR QUALITY (Windsor)	1.4 - 3.4	$2.0 \times 10^{-6}$ $4.9 \times 10^{-5}$	EPA	$9.1 \times 10^{-2}$ (a)	$1.8 \times 10^{-4}$ - $4.5 \times 10^{-4}$
			CDHS	$7 \times 10^{-2}$ (a)	$1.4 \times 10^{-4}$ - $3.4 \times 10^{-4}$
			WHO	None proposed	
			OVERALL RANGE OF RISKS: $1.4 \times 10^{-4}$ - $4.5 \times 10^{-4}$		
TYPICAL OUTDOOR EXPOSURE (ie.= 3 hr.)	0.2 - 0.4	$2.9 \times 10^{-4}$ $5.7 \times 10^{-4}$	EPA	$9.1 \times 10^{-2}$ (a)	$2.6 \times 10^{-7}$ - $5.2 \times 10^{-7}$
			CDHS	$7 \times 10^{-2}$ (a)	$2.0 \times 10^{-7}$ - $4.0 \times 10^{-7}$
			WHO	None proposed	
			OVERALL RANGE OF RISKS: $2.0 \times 10^{-7}$ - $5.2 \times 10^{-7}$		
INDOOR AIR ENVIRONMENTS (Extended periods of exposure expected)	19.3 - 26.3	$2.8 \times 10^{-4}$ - $3.8 \times 10^{-4}$	EPA	$9.1 \times 10^{-2}$ (a)	$2.6 \times 10^{-5}$ - $3.5 \times 10^{-5}$
			CDHS	$7 \times 10^{-2}$ (a)	$2.0 \times 10^{-5}$ - $2.7 \times 10^{-5}$
			WHO	None proposed	
			OVERALL RANGE OF RISKS: $2.0 \times 10^{-5}$ - $3.5 \times 10^{-5}$		
a. These are equivalent potency factors calculated from the unit risks proposed by the agencies listed; assumed adult weight of 70 kg and 20 m <sup>3</sup> per day.					

#### Summary and recommendations:

- ♦ All exposures are less than the range of chronic acceptable exposure levels. Therefore, the possibility of long-term health effects, other than cancer risk, is unlikely.
- ♦ Since the levels of inhalation risk in indoor environments exceed  $1 \times 10^{-5}$ , a level generally deemed to be negligible, this is an area where exposure reduction for ethylene dichloride is recommended.

#### REFERENCES

1. Agency for Toxic Substances and Disease Registry, U.S. Public Health Service. Toxicological Profile for 1,2-Dichloroethane (Draft). October 1992.

**APPENDIX 14**  
**RISK ANALYSIS FOR CHLOROFORM**





## CHLOROFORM

### NATURE of the CHEMICAL, SOURCES, LEVELS in OUTDOOR and INDOOR AIR, and ESTIMATED INTAKES.

Chloroform (trichloromethane) is a colourless, volatile liquid at room temperature and pressure, with a pleasant odour. It is widely used in the manufacture of fluorocarbons, pesticides, and dyes; as a solvent; and as a drycleaning spot remover. Chloroform is released to the environment from both biogenic and anthropogenic sources, however, the latter is the major contributor. The anthropogenic sources include evaporation during the chlorination of pulp by pulp and paper mills, chlorination of wastewater from sewage treatment plants, chlorination of drinking water, emissions from pharmaceutical and chemical manufacturing plants. Because of this, ambient air concentrations are generally higher in urban areas than rural.

**Table 1. Levels of Chloroform in Outdoor and Indoor Air in Windsor and, Estimated Intakes per day (in ug/day) Associated with these Environments.**

ENVIRONMENTS	Concentration Mean or Range of Means  ug/m <sup>3</sup>	Concentration 90th percentile (or Range of)  ug/m <sup>3</sup>	Estimated Adult Range of Intakes per day  ug/day
Outdoor Air Quality - Windsor (ie. 100 % outdoor exposure) (a)	0.15	0.29	3 - 5.8 (a),(d)
Typical outdoor exposure (ie. ~ 3hr) (b)	0.15	0.29	0.4 - 0.7 (b)
INDOOR AIR ENVIRONMENTS (c) (EXTENDED periods of exposure expected) (e.g. Home, office)	1.8 - 4.6	4.1 - 13.2	31.5 - 231 (e)
INDOOR AIR ENVIRONMENTS (c) (BRIEF periods of exposure expected) (e.g. Commuting, bingo halls, taverns)	15.9	30 (g)	Not included (f)

a) Based on 224, 24 hour average samples. Range of intakes is associated with the range of the 'mean' to '90th percentile' concentrations in outdoor air. It is to be noted that people are not exposed 24 hours to outdoor air. This estimation assumes 100 % exposure to outdoor air and is a measure of outdoor air quality per se and not of actual exposure.

b) Range of intakes calculated from the 'mean' to '90th percentile' concentrations in outdoor air and assuming a 'typical' outdoor air exposure of ~ 3 hr (ie. corresponding to breathing 2.5 m<sup>3</sup>/3hr for adults).

c) From the Windsor personal exposure & microenvironment studies

d) Assuming an inhalation rate of 20 m<sup>3</sup>/day

e) Range of intakes is estimated from the range of the lowest 'mean' and the highest '90th percentile' concentrations obtained from personal exposure and microenvironment measurements in indoor environments in environments where extended periods of exposure are expected. A total exposure of 21 hours (ie. 17.5 m<sup>3</sup>/day) was assumed for these indoor environments.

f) Direct estimation of daily intake is not appropriate since relatively small amounts of time is spent in these microenvironments

g) A range of 4.9(minimum) - 74(maximum) ug/m<sup>3</sup> was observed in a limited data set in the 'commuting' environment; also a single value of 39.9 ug/m<sup>3</sup> was observed on an indoor swimming pool deck;

Average (ie. 'mean') and 90th percentile concentrations (or range of concentrations) of chloroform in outdoor and indoor air are summarized in Table 1. Estimated adult intakes per day in units of ug/day,

associated with these concentrations, are also included in Table 1.

## HEALTH CONCERNS

Both short-term and long-term exposures to levels at or above 25 ppm (124000 ug/m<sup>3</sup>) have been associated with toxic effects in both animals and humans. These effects include liver and kidney toxicity and depression of the central nervous system. However, these levels of chloroform which cause adverse health effects are much higher than the concentrations measured in the environment.

The cancer causing potential of chloroform has been examined in several animal studies. It has been shown to cause kidney tumors in rats and liver and kidney tumors in mice. The U.S. EPA ranks chloroform as a probable human carcinogen.

Various health criteria (ie. Unit risks, Reference concentrations, ambient air quality guidelines) from lead agencies are summarized in Table 2. The table also includes the calculated "allowable" intake associated with the listed health criteria.

## RISK CHARACTERIZATION AND PERSPECTIVES

From the brief exposure analysis and the available health criteria the following observations can be made:

### Health messages:

- 1) All exposures are less than the chronic acceptable exposure level (ie. 700 ug/day) proposed by California (CDHS).
- 2) The most conservative exposure guidelines available are the potencies shown in Table 3. The carcinogenic risk associated with 'outdoor air quality' (ie. 100 % outdoor exposure) is between  $7.7 \times 10^{-7}$  and  $6.7 \times 10^{-6}$ . Similarly the risk associated with 'typical outdoor exposures' (ie. 3 hr) is between  $1.0 \times 10^{-7}$  and  $8.1 \times 10^{-7}$ . Similarly the range of risks associated with indoor air environments (ie. those in which extended periods of exposure are expected) is between  $8.1 \times 10^{-6}$  and  $2.7 \times 10^{-4}$ . The risks associated with indoor air environments (ie. those in which extended periods of exposure are expected) are slightly higher than the risks associated with 'outdoor air quality' which in turn is higher than 'typical outdoor exposures'. It should be noted that this risk characterization (ie. using carcinogenic based limits) is based on an assumed lifetime exposure (ie. 24 hours, every day, for 70 years) and hence is a very conservative assumption.
- 3) Exposures associated with indoor environments (ie. those in which extended periods of exposure are expected) exceed those associated with typical outdoor air exposures (ie. 3 hr).

### Regulatory compliance messages:

- 4) All exposures associated with outdoor air quality (ie. 100 % outdoor exposure) and typical outdoor exposure (ie. 3 hr) fall in the lower 2 % range of air quality guidelines of various jurisdictions. Exposures associated with indoor air environments (ie. those in which extended periods of exposure are expected) fall in the lower 50 % range of air quality guidelines of various jurisdictions. All exposures are less than the Ontario guideline.
- 5) All exposures are less than the range of occupational levels.

TABLE 2. Summary of Exposure Guidelines for Chloroform from Leading Agencies

GUIDELINE APPLICATION	AGENCY(IES)	ORIGINAL VALUE	CONCENTRATION ("Original Form" converted to these -as applicable)			CALCULATED "ALLOWABLE" INTAKE (3)
			Unit Risk (1)	RsC (2) (1 x 10 <sup>-6</sup> )	RsC (2) (1 x 10 <sup>-6</sup> )	
INHALATION GUIDELINES						
Occupational	ACGIH, Ontario	49000 ug/m <sup>3</sup>	NA	NA	NA	980000 (14)
Ambient Air Quality Guidelines	US states,	0.04 - 23 ug/m <sup>3</sup>	NA	NA	NA	0.8 - 460 (1.1 x 10 <sup>-6</sup> - 6.6 x 10 <sup>-6</sup> )
Air Quality Guideline	Ontario	500 ug/m <sup>3</sup>	NA	NA	NA	10000 (0.14)
Chronic AELs/RfCs	CDHS WHO	35 ug/m <sup>3</sup> NA	NA	NA	NA	700 (0.01) NA
Inhalation Cancer Potency Factor	EPA CDHS WHO	See Unit Risk column	2.3 x 10 <sup>-4</sup> 5.3 x 10 <sup>-4</sup> NA	0.4 1.9 NA	0.04 0.2 NA	for 1 x 10 <sup>-4</sup> risk: 8 - 38 (1.1 x 10 <sup>-6</sup> - 5.4 x 10 <sup>-6</sup> ) for 1 x 10 <sup>-6</sup> risk: 0.8 - 4 (1.1 x 10 <sup>-6</sup> - 5.7 x 10 <sup>-6</sup> )

<sup>1</sup>For inhalation guidelines, unit risks are expressed as (ug/m<sup>3</sup>)<sup>-1</sup><sup>2</sup>For inhalation guidelines, risk specific concentrations are expressed as ug/m<sup>3</sup><sup>3</sup>Intake was computed by assuming, where applicable, an adult weight of 70 kg, a breathing rate of 20 m<sup>3</sup>/day. In all cases 100% bioavailability of the intake was assumed.

Table 3. Range of Inhalation Cancer Risks Associated with Estimated Intakes(ie. for adult exposures only) of Chloroform

RANGE of INHALATION INTAKES			POTENCY (a)		RANGE of RISKS
Environment	Unit ug/day	Unit mg/kg/day	Agency	Unit (mg/kg-d) <sup>a</sup>	
OUTDOOR AIR QUALITY (Windsor)	3 - 5.8	$4.3 \times 10^{-5}$ $8.3 \times 10^{-5}$	EPA	0.081 (a)	$3.5 \times 10^{-4}$ - $6.7 \times 10^{-4}$
			CDHS	0.018(a)	$7.7 \times 10^{-7}$ - $1.5 \times 10^{-4}$
			WHO	None proposed	
			OVERALL RANGE OF RISKS: $7.7 \times 10^{-7}$ - $6.7 \times 10^{-4}$		
TYPICAL OUTDOOR EXPOSURE (ie. 3 hr.)	0.4 - 0.7	$5.7 \times 10^{-4}$ $1.0 \times 10^{-5}$	EPA	0.081(a)	$4.7 \times 10^{-7}$ - $8.1 \times 10^{-7}$
			CDHS	0.018 (a)	$1.0 \times 10^{-7}$ - $1.8 \times 10^{-7}$
			WHO	None proposed	
			OVERALL RANGE OF RISKS: $1.0 \times 10^{-7}$ - $8.1 \times 10^{-7}$		
INDOOR AIR ENVIRONMENTS (Extended periods of exposure expected)	31.5 - 231	$4.5 \times 10^{-4}$ - $3.3 \times 10^{-3}$	EPA	0.081(a)	$3.6 \times 10^{-5}$ - $2.7 \times 10^{-4}$
			CDHS	0.018(a)	$8.1 \times 10^{-4}$ - $5.9 \times 10^{-5}$
			WHO	None proposed	
			OVERALL RANGE OF RISKS: $8.1 \times 10^{-4}$ - $2.7 \times 10^{-4}$		
a. These are equivalent potency factors calculated from the unit risks proposed by the agencies listed; assumed adult weight of 70 kg and 20 m <sup>3</sup> per day.					

6) MOEE will be reviewing the basis of the existing standard for chloroform.

#### Summary and recommendations:

- ♦ All exposures are less than the range of chronic acceptable exposure levels. Therefore, the possibility of long-term health effects, other than cancer risk, is unlikely.
- ♦ Since the levels of inhalation risk in indoor environments exceed  $1 \times 10^{-5}$ , a level generally deemed to be negligible, this is an area where exposure reduction for chloroform is recommended.

#### REFERENCES

1. Agency for Toxic Substances and Disease Registry, U.S. Public Health Service. Toxicological Profile for Chloroform. January 1989.

**APPENDIX 15**

**RISK ANALYSIS FOR ETHYLENE DIBROMIDE**





## ETHYLENE DIBROMIDE

### NATURE of the CHEMICAL, SOURCES, LEVELS in OUTDOOR and INDOOR AIR, and ESTIMATED INTAKES.

Ethylene dibromide (EDB; 1,2-dibromoethane) is a nonflammable, colourless, volatile liquid at room temperature and pressure, with a sweet odour. A major use of ethylene dibromide is as an additive to scavenge for lead in leaded gasoline, however, the use of leaded gasoline is declining; a minor use is to control pests; as a chemical intermediate in the synthesis of dyes; and as a solvent for resins, gums, and waxes. It is released to the environment from biogenic and anthropogenic sources, although, the latter is by far the major contributor. The anthropogenic sources include fugitive emissions from leaded gasolines, automobile exhaust, and emission from facilities that manufacture and process ethylene dibromide. Because of this, ambient air concentrations are generally higher in urban areas than rural.

Average (ie. 'mean') and 90th percentile concentrations (or range of concentrations) of ethylene dibromide in outdoor and indoor air are summarized in Table 1. Estimated adult intakes per day in units of ug/day, associated with these concentrations, are also included in Table 1.

**Table 1. Levels of Ethylene dibromide in Outdoor and Indoor Air in Windsor and, Estimated Intakes per day (in ug/day) Associated with these Environments.**

ENVIRONMENTS	Concentration Mean or Range of Means  ug/m <sup>3</sup>	Concentration 90th percentile (or Range of)  ug/m <sup>3</sup>	Estimated Adult Range of Intakes per day  ug/day
Outdoor Air Quality - Windsor (ie. 100 % outdoor exposure) (a)	Not available	0.42 (e)	8.4 (a) ,(d)
Typical outdoor exposure (ie. ~ 3hr) (b)	Not available	0.42 (e)	1.1 (b)
INDOOR AIR ENVIRONMENTS (c) (EXTENDED periods of exposure expected) (e.g. Home, office)	Not available	Not available	Not available
INDOOR AIR ENVIRONMENTS (c) (BRIEF periods of exposure expected) (e.g. Commuting, bingo halls, taverns)	Not available	Not available	Not available

a) Based on 224, 24 hour average samples. EDB was detected in only 8 samples. The intake shown is associated with the maximum concentration (ie. only maximum value available in view of the small number of samples in which EDB was detected) in outdoor air. It is to be noted that people are not exposed 24 hours to outdoor air. This estimation assumes 100 % exposure to outdoor air and is a measure of outdoor air quality per se and not of actual exposure.

b) The intake calculated from the maximum concentration in outdoor air and assuming a 'typical' outdoor air exposure of ~ 3 hr(ie. corresponding to breathing 2.5 m<sup>3</sup>/3hr for adults).

c) No data on EDB was available from the Windsor personal exposure & microenvironment studies

d) Assuming an inhalation rate of 20 m<sup>3</sup>/day

e) This is a maximum value.

## HEALTH CONCERNS

Both short-term and long-term exposures to levels above 3 ppm (ie.  $>23040 \text{ ug/m}^3$ ) have been associated with toxic effects in both animals and humans. These effects include eye irritation and damage to the lungs, nasal cavity, spleen, kidneys, and liver. However, these levels of chloroform which cause adverse health effects are much higher than the concentrations measured in the environment.

The cancer causing potential of ethylene dibromide has been examined in several animal studies. It has been shown to cause tumors of the spleen, mammary glands, nasal cavity and lungs in rats and tumors of the ovaries, uterus, kidneys, adrenal glands, nasal cavity and lungs in mice. U.S. EPA ranks ethylene dibromide as a probable human carcinogen.

Various health criteria (ie. Unit risks, Reference concentrations, ambient air quality guidelines) from lead agencies are summarized in Table 2. The table also includes the calculated "allowable" intake associated with the listed health criteria.

## RISK CHARACTERIZATION AND PERSPECTIVES

From the brief exposure analysis and the available health criteria the following observations can be made:

### Health messages:

1) All exposures are less than the chronic acceptable exposure level (ie.  $92 \text{ ug/day}$ ) proposed by California (CDHS).

2) The most conservative exposure guidelines available are the potencies shown in Table 3. The carcinogenic risk associated with 'outdoor air quality' (ie. 100 % outdoor exposure) is between  $3.0 \times 10^{-5}$  and  $9.2 \times 10^{-5}$ . Similarly the risk associated with 'typical outdoor exposures' (ie. 3 hr) is between  $1.2 \times 10^{-5}$  and  $4 \times 10^{-6}$ . The risks associated with 'outdoor air quality' are slightly higher than the risks associated with 'typical outdoor exposures'. These risk estimates should be interpreted with utmost care since they are based on maximum values in 8 samples, while 216 samples showed no detectable levels of ethylene dibromide. If the risk estimates were based on the detection limit, they would be reduced by at least 4-fold, but could be even lower. It should also be noted that this risk characterization (ie. using carcinogenic based limits) is based on an assumed lifetime exposure (ie. 24 hours, every day, for 70 years) and hence is a very conservative assumption.

### Regulatory compliance messages:

3) All exposures associated with outdoor air quality (ie. 100 % outdoor exposure) and typical outdoor exposure (ie. 3 hr) overlap with and slightly exceed the air quality guidelines of various jurisdictions. It is to be noted that these exposures are based on maximum concentrations that were measured during the few times that the substance was detected (ie. detected only 8 times out of 224 samples). These exposures are less than the Ontario Approvals Screening Level (ie. an Ontario guideline) for EDB. In indoor environments EDB was not detected.

4) Occupational exposure limits have not been established and hence comparison is not possible.

TABLE 2. Summary of Exposure Guidelines for Ethylene dibromide from Leading Agencies

GUIDELINE APPLICATION	AGENCY(IES)	ORIGINAL VALUE	CONCENTRATION ("Original Form" converted to these -as applicable)			CALCULATED "ALLOWABLE" INTAKE (3)
			Unit Risk (1)	R <sub>SC</sub> (2) (1 x 10 <sup>-6</sup> )	R <sub>SC</sub> (2) (1 x 10 <sup>-6</sup> )	
INHALATION GUIDELINES						
Occupational	ACGIH, Ontario	NA	NA	NA	NA	NA
Ambient Air Quality Guidelines	US states,	0.004-0.4 ug/m <sup>3</sup>	NA	NA	NA	0.08 - 8 (1.1 x 10 <sup>-6</sup> - 1.1 x 10 <sup>-4</sup> )
Air Quality Guideline	Ontario <sup>a</sup>	3 ug/m <sup>3</sup>	NA	NA	NA	60 (8.6 X 10 <sup>-4</sup> )
Chronic AELs/RfCs	CDHS WHO	4.6 ug/m <sup>3</sup> NA	NA	NA	NA	92 (1.3 x 10 <sup>-3</sup> ) NA
Inhalation Cancer Potency Factor	EPA CDHS WHO	See Unit Risk column	2.2 x 10 <sup>-4</sup> 7.1 x 10 <sup>-4</sup> NA	0.05 0.14 NA	0.005 0.014 NA	for 1 x 10 <sup>-4</sup> risk: 1 - 2.8 (1.4 x 10 <sup>-4</sup> - 4 x 10 <sup>-3</sup> ) for 1 x 10 <sup>-4</sup> risk: 0.1 - 0.28 (1.4 x 10 <sup>-4</sup> - 4 x 10 <sup>-3</sup> )

<sup>1</sup>For inhalation guidelines, unit risks are expressed as (ug/m<sup>3</sup>)<sup>-1</sup>

<sup>2</sup>For inhalation guidelines, risk specific concentrations are expressed as ug/m<sup>3</sup>

<sup>3</sup>Intake was computed by assuming, where applicable, an adult weight of 70 kg a breathing rate of 20 m<sup>3</sup>/day. In all cases 100% bioavailability was assumed.

<sup>4</sup>This is an Approvals Screening Level (ASL).

Table 3. Range of Inhalation Cancer Risks Associated with Estimated Intakes(ie. for adult exposures only) of Ethylene Dibromide

RANGE of INHALATION INTAKES			POTENCY (a)		RANGE of RISKS
Environment	Unit ug/day	Unit mg/kg/day	Agency	Unit (mg/kg-d) <sup>1</sup>	
OUTDOOR AIR QUALITY (Windsor)	8.4	$1.2 \times 10^{-4}$	EPA	0.77 (a)	$9.2 \times 10^{-5}$
			CDHS	0.25 (a)	$3 \times 10^{-5}$
			WHO	None proposed	NA
			OVERALL RANGE OF RISKS: $3 \times 10^{-5}$ - $9.2 \times 10^{-5}$		
TYPICAL OUTDOOR EXPOSURE (ie. = 3 hr.)	1.1	$1.6 \times 10^{-5}$	EPA	0.77 (a)	$1.2 \times 10^{-5}$
			CDHS	0.25 (a)	$4 \times 10^{-6}$
			WHO	None proposed	NA
			OVERALL RANGE OF RISKS: $1.2 \times 10^{-5}$ - $4 \times 10^{-6}$		
INDOOR AIR ENVIRONMENTS (Extended periods of exposure expected)	Not Available	NA	EPA	0.77 (a)	NA
			CDHS	0.25 (a)	NA
			WHO	None proposed	NA
			OVERALL RANGE OF RISKS: NA		

a. These are equivalent potency factors calculated from the unit risks proposed by the agencies listed; assumed adult weight of 70 kg and 20 m<sup>3</sup> per day.

#### Summary and recommendations:

- ♦ All exposures are less than the range of chronic acceptable exposure levels. Therefore, the possibility of long-term health effects, other than cancer risk, is unlikely.
- ♦ Since the levels of inhalation risk are likely less than  $1 \times 10^{-5}$ , a level generally deemed to be negligible, it is not necessary to place a high priority on exposure reduction for ethylene dibromide.

#### REFERENCES

1. Agency for Toxic Substances and Disease Registry, U.S. Public Health Service. Toxicological Profile for 1,2-Dibromoethane (Draft). October 1990.



## APPENDIX 16

### RISK ANALYSIS FOR TRICHLOROETHYLENE



## TRICHLOROETHYLENE

### NATURE of the CHEMICAL, SOURCES, LEVELS in OUTDOOR and INDOOR AIR, and ESTIMATED INTAKES.

Trichloroethylene is a non-flammable, colourless, volatile liquid that possesses an odour similar to that of chloroform or diethyl ether. As with virtually all chlorinated organic compounds, there are no natural sources of trichloroethylene.

Trichloroethylene is used primarily as a solvent for removing grease from metal parts. It is also used as a solvent in many products such as adhesives, correction fluids, lubricants, paints, varnishes, paint strippers and pesticide formulations. In the textile industry, trichloroethylene may be used to remove fats and oils from natural fibres (cotton, wool, etc.), in dyeing and in finishing operations. Trichloroethylene is also used as an intermediate in the synthesis of other chemicals, including PVC. In the past, it was used as a general anaesthetic and as a solvent for extracting caffeine from coffee, however these applications have been abandoned<sup>1</sup>.

The major route of trichloroethylene's entry to the environment is through its evaporation when used as a degreasing solvent. Most of the substance ends up in the air although it may be present as a contaminant of surface water and groundwater<sup>1</sup>.

Average (ie. 'mean') and 90th percentile concentrations (or range of concentrations) of trichloroethylene in outdoor and indoor air are summarized in Table 1. Estimated adult intakes per day in units of ug/day, associated with these concentrations, are also included in Table 1.

**Table 1. Levels of Trichloroethylene in Outdoor and Indoor Air in Windsor and, Estimated Intakes per day (in ug/day) Associated with these Environments.**

ENVIRONMENTS	Concentration Mean or Range of Means  ug/m <sup>3</sup>	Concentration 90th percentile (or Range of)  ug/m <sup>3</sup>	Estimated Adult Range of Intakes per day  ug/day
Outdoor Air Quality - Windsor (ie. 100 % outdoor exposure) (a)	0.3	0.69	6 - 13.8 (a) (d)
Typical outdoor exposure (ie. ~ 3hr) (b)	0.3	0.69	0.8 - 1.7 (b)
INDOOR AIR ENVIRONMENTS (c) (EXTENDED periods of exposure expected) (e.g. Home, office)	0.9 - 1.3	3.2 - 3.9	15.8 - 68.3 (e)
INDOOR AIR ENVIRONMENTS (c) (BRIEF periods of exposure expected) (e.g. Commuting, bingo halls, taverns)	0.4 (g)	36 (h)	Not included (f)

- a) Based on 225, 24 hour average samples. Range of intakes is associated with the range of the 'mean' to '90th percentile' concentrations in outdoor air. It is to be noted that people are not exposed 24 hours to outdoor air. This estimation assumes 100 % exposure to outdoor air and is a measure of outdoor air quality per se and not of actual exposure.
- b) Range of intakes calculated from the 'mean' to '90th percentile' concentrations in outdoor air and assuming a 'typical' outdoor air exposure of  $\approx 3$  hr (ie. corresponding to breathing  $2.5 \text{ m}^3/\text{hr}$  for adults).
- c) From the Windsor personal exposure & microenvironment studies
- d) Assuming an inhalation rate of  $20 \text{ m}^3/\text{day}$
- e) Range of intakes is estimated from the range of the lowest 'mean' and the highest '90th percentile' concentrations obtained from personal exposure and microenvironment measurements in indoor environments in environments where extended periods of exposure are expected. A total exposure of 21 hours (ie.  $17.5 \text{ m}^3/\text{day}$ ) was assumed for these indoor environments.
- f) Direct estimation of daily intake is not appropriate since relatively small amounts of time is spent in these microenvironments
- g) This is a minimum value.
- h) This is a maximum value.

## HEALTH CONCERNS

Short-duration exposure to trichloroethylene vapour can cause nose and throat irritation at levels as low as 30 ppm, and levels of 100-600 ppm can cause depression of the central nervous system with symptoms such as dizziness, headache, vertigo, nausea and fatigue. Above 1000 ppm, there may be loss of consciousness, tremors, loss of coordination and visual disorders. Long-term exposure to trichloroethylene in an occupational setting (levels above 200 ppm) has been associated with liver damage, and possibly also damage to the central nervous system resulting in tremors, dizziness, slowed heart rate, numbness in the hands, anxiety, insomnia and behavioural problems<sup>4,5</sup>.

Note however that all of the concentrations above are far in excess of the ppb levels expected to be found in ambient air (average 1 ppb, maximum 32 ppb). The effects described above would be very unlikely to occur upon exposure to trichloroethylene in ambient air<sup>2</sup>.

There is evidence that trichloroethylene can cause cancer in animals, including the results of three studies showing liver cancer in one strain of mouse, one study showing lymphatic cancer in a different strain of mouse, and one study showing kidney cancer in rats. With regard to humans, the information available to date is inconclusive. Based on animal data, it appears that trichloroethylene may be a low-potency, potential human carcinogen. Because of inconsistencies in the data from cancer studies, the U.S. EPA has not yet decided whether the substance is a "probable" or "possible" human carcinogen<sup>1,2,3</sup>.

Various health-based criteria (e.g. unit risks, reference concentrations, ambient air quality guidelines) from leading regulatory and advisory agencies are summarized in Table 2. The table also includes the calculated "allowable" intake associated with the listed health criteria.

## RISK CHARACTERIZATION AND PERSPECTIVES

From the brief exposure analysis and the available health criteria the following observations can be made:

### Health messages:

- 1) All exposures are less than the range of chronic acceptable exposure levels (ie. 12800 - 20000  $\mu\text{g}/\text{day}$ ) proposed by California (CDHS) and the WHO.

TABLE 2 Summary of Exposure Guidelines for Trichloroethylene from Leading Agencies

GUIDELINE APPLICATION	AGENCY(IES)	ORIGINAL VALUE	CONCENTRATION ("Original Form" converted to these -as applicable)			CALCULATED "ALLOWABLE" INTAKE (3)
			Unit Risk (1)	R <sub>s</sub> C (2) (1 x 10 <sup>-4</sup> )	R <sub>s</sub> C (2) (1 x 10 <sup>-4</sup> )	
INHALATION GUIDELINES						
Occupational	ACGIH, Ontario	268000-269000 ug/m <sup>3</sup>	NA	NA	NA	5360000-5380000 (76.6-76.9)
Ambient Air Quality Guidelines	U.S. States	0.059-135 ug/m <sup>3</sup>	NA	NA	NA	1.2-2700 (0.00002-0.04)
Air Quality Guideline	Ontario	28000 ug/m <sup>3</sup>	NA	NA	NA	560000 (8)
Chronic AELs/RfCs	CDHS WHO	640 ug/m <sup>3</sup> 1000 ug/m <sup>3</sup>	NA	NA	NA	12800 (0.18) 20000 (0.29)
Inhalation Cancer Potency Factor	EPA CDHS WHO	See Unit Risk column	(under review) 2 x 10 <sup>-4</sup> none provided	5	0.5	for 1 x 10 <sup>-4</sup> risk: 100 (0.0014) for 1 x 10 <sup>-6</sup> risk: 10 (0.00014)

<sup>1</sup>For inhalation guidelines, unit risks are expressed as (ug/m<sup>3</sup>)<sup>-1</sup><sup>2</sup>For inhalation guidelines, risk specific concentrations are expressed as ug/m<sup>3</sup><sup>3</sup>Intake was computed by assuming, where applicable, an adult weight of 70 kg, a breathing rate of 20 m<sup>3</sup>/day. In all cases 100% bioavailability of the intake was assumed.



2) The most conservative exposure guideline available is California's cancer potency-based value shown in Table 3 (a similar value developed by the U.S. EPA was withdrawn pending review). The carcinogenic risk associated with 'outdoor air quality' (ie. 100 % outdoor exposure) is between  $6 \times 10^{-10}$  and  $1.4 \times 10^{-9}$ . Similarly the risk associated with 'typical outdoor exposures' (ie. 3 hr) is between  $7.7 \times 10^{-11}$  and  $1.7 \times 10^{-10}$ . Similarly the range of risks associated with indoor air environments (ie. those in which extended periods of exposure are expected) is between  $1.6 \times 10^{-9}$  and  $6.9 \times 10^{-9}$ . The risks associated with indoor air environments (ie. those in which extended periods of exposure are expected) are slightly higher than the risks associated with 'outdoor air quality' which in turn is higher than 'typical outdoor exposures'. It should be noted that this risk characterization (ie. using carcinogenic based limits) is based on an assumed lifetime exposure (ie. 24 hours, every day, for 70 years) and hence is a very conservative assumption.

3) Exposures associated with indoor environments (ie. those in which extended periods of exposure are expected) exceed those associated with typical outdoor air exposures (ie. 3 hr).

#### Regulatory compliance messages:

4) All exposures associated with outdoor air quality (ie. 100 % outdoor exposure) and typical outdoor exposure (ie. 3 hr) fall in the lower 1 % range of air quality guidelines of various jurisdictions. Exposures associated with indoor air environments (ie. those in which extended periods of exposure are expected) fall in the lower 3 % range of air quality guidelines of various jurisdictions. All exposures are less than the Ontario guideline.

5) All exposures fall far below the range of occupational levels.

**Table 3. Range of Inhalation Cancer Risks Associated with Estimated Intakes (ie. for adult exposures only) of Trichloroethylene**

RANGE of INHALATION INTAKES			POTENCY (a)		RANGE of RISKS
Environment	Unit ug/day	Unit mg/kg/day	Agency	Unit (mg/kg-d) <sup>-1</sup>	
OUTDOOR AIR QUALITY (Windsor)	6 - 13.8	$8.6 \times 10^{-5}$ $2.0 \times 10^{-4}$	EPA	N.A.	
			CDHS	$7 \times 10^{-4}$ (a)	$6.0 \times 10^{-10}$ - $1.4 \times 10^{-9}$
			WHO	None proposed	
			OVERALL RANGE OF RISKS: $6.0 \times 10^{-10}$ - $1.4 \times 10^{-9}$		
TYPICAL OUTDOOR EXPOSURE (ie. 3 hr.)	0.8 - 1.7	$1.1 \times 10^{-5}$ $2.4 \times 10^{-5}$	EPA	N.A.	
			CDHS	$7 \times 10^{-4}$ (a)	$7.7 \times 10^{-11}$ - $1.7 \times 10^{-10}$
			WHO	None proposed	
			OVERALL RANGE OF RISKS: $7.7 \times 10^{-11}$ - $1.7 \times 10^{-10}$		
INDOOR AIR ENVIRONMENTS (Extended periods of exposure expected)	15.8 - 68.3	$2.3 \times 10^{-4}$ - $9.8 \times 10^{-4}$	EPA	N.A.	
			CDHS	$7 \times 10^{-4}$ (a)	$1.6 \times 10^{-9}$ - $6.9 \times 10^{-9}$
			WHO	None proposed	
			OVERALL RANGE OF RISKS: $1.6 \times 10^{-9}$ - $6.9 \times 10^{-9}$		

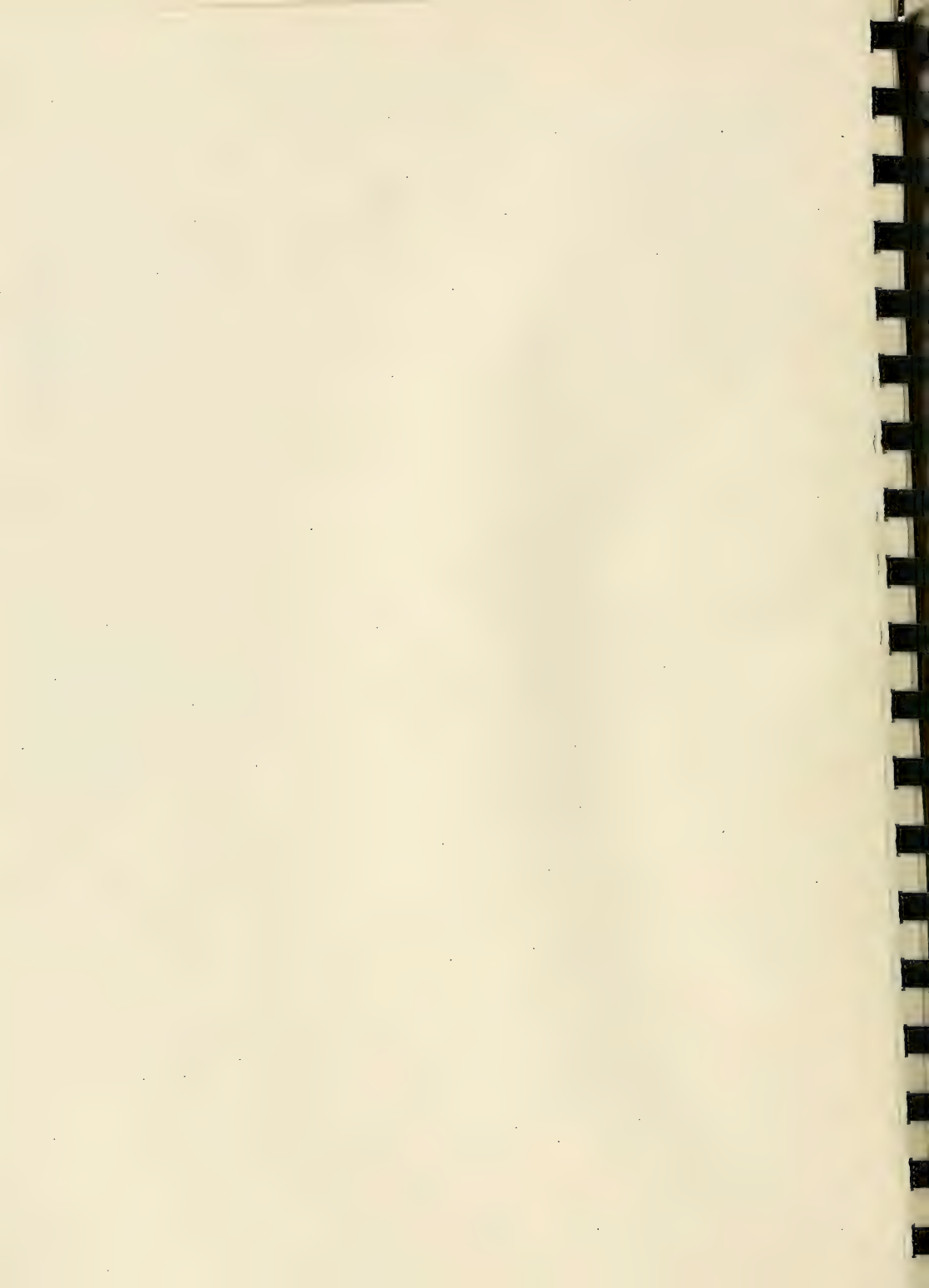
a. These are equivalent potency factors calculated from the unit risks proposed by the agencies listed; assumed adult weight of 70 kg and 20 m<sup>3</sup> per day.

#### Summary and recommendations:

- ♦ All exposures are less than the range of chronic acceptable exposure levels. Therefore, the possibility of long-term health effects, other than cancer risk, is unlikely.
- ♦ Since the levels of inhalation risk are considerably less than  $1 \times 10^{-5}$ , a level generally deemed to be negligible, it is not necessary to place a priority on exposure reduction for trichloroethylene.

#### REFERENCES

1. Agency for Toxic Substances and Disease Registry, U.S. Public Health Service. Toxicological Profile for Trichloroethylene (draft). October 1991.
2. United States Environmental Protection Agency, Office of Health and Environmental Assessment. Health Assessment Document for Trichloroethylene. July 1985.
3. United States Environmental Protection Agency, Office of Health and Environmental Assessment. Health Assessment Document for Trichloroethylene July 1987 Draft Addendum. March 1988.
4. United Kingdom Health and Safety Executive. Toxicity Review: Trichloroethylene. 1982.
5. Canadian Centre for Occupational Health and Safety. CHEMINFO file on trichloroethylene. January 1987.



**APPENDIX 17**  
**RISK ANALYSIS FOR NICKEL**





## NICKEL

### NATURE of the CHEMICAL, SOURCES, LEVELS in OUTDOOR and INDOOR AIR, and ESTIMATED INTAKES.

Nickel, a metallic element, is mostly used for the production of stainless steel and other nickel alloys with high corrosion and temperature resistance. Nickel alloys and nickel plating are used in vehicles, processing machinery, armaments, tools, electrical equipment, medical equipment, household appliances, pigments in glassware and ceramics and coinage. The main anthropogenic sources of nickel emission into the ambient air are the combustion of coal and oil for heating or power generation, the incineration of waste and sewage sludge, nickel mining and primary production, steel manufacturing, electroplating and other sources such as cement manufacturing. In the polluted air, the predominant nickel compounds appear to be nickel sulphate, oxides and sulphides and to a lesser extent, metallic nickel. Atmospheric nickel exists mainly in particulate aerosols and the highest concentrations in the ambient air are usually found in the smallest particles. Nickel carbonyl, formed during the carbon monoxide based refining of impure metal, is not stable in the ambient environment and it readily decomposes to nickel oxide.

Average (ie. 'mean') and 90th percentile concentrations (or range of concentrations) of Nickel in outdoor and indoor air are summarized in Table 1. Estimated adult intakes per day in units of ug/day, associated with these concentrations, are also included in Table 1.

**Table 1. Levels of Nickel in Outdoor and Indoor Air in Windsor and, Estimated Intakes per day (in ug/day) Associated with these Environments.**

ENVIRONMENTS	Concentration Mean or Range of Means  ng/m <sup>3</sup>	Concentration 90th percentile (or Range of)  ng/m <sup>3</sup>	Estimated Adult Range of Intakes per day  ug/day
Outdoor Air Quality - Windsor (ie. 100 % outdoor exposure) (a)	4	10	0.08 - 0.2 (a), (d)
Typical outdoor exposure (ie. ~ 3hr) (b)	4	10	0.01 - 0.03 (b)
INDOOR AIR ENVIRONMENTS (c) (EXTENDED periods of exposure expected) (e.g. Home, office)	1 - 1.6	1.7 - 2.1	0.02 - 0.04 (e)
INDOOR AIR ENVIRONMENTS (c) (BRIEF periods of exposure expected) (e.g. Commuting, bingo halls, taverns)	1.1 - 1.9	1.4 - 2.9	Not included (f)

- a) Based on 2839, 24 hour average samples (ie. in total suspended particulate -TSP), acquired over several years from several sites in Windsor. Range of intakes is associated with the range of the 'mean' to '90th percentile' concentrations in outdoor air. It is to be noted that people are not exposed 24 hours to outdoor air. This estimation assumes 100 % exposure to outdoor air and is a measure of outdoor air quality per se and not of actual exposure.
- b) Range of intakes calculated from the 'mean' to '90th percentile' concentrations in outdoor air and assuming a 'typical' outdoor air exposure of  $\approx 3$  hr (ie. corresponding to breathing  $2.5 \text{ m}^3/\text{hr}$  for adults).
- c) From the Windsor personal exposure & microenvironment studies
- d) Assuming an inhalation rate of  $20 \text{ m}^3/\text{day}$
- e) Range of intakes is estimated from the range of the lowest 'mean' and the highest '90th percentile' concentrations obtained from personal exposure and microenvironment measurements in indoor environments in environments where extended periods of exposure are expected. A total exposure of 21 hours (ie.  $17.5 \text{ m}^3/\text{day}$ ) was assumed for these indoor environments.
- f) Direct estimation of daily intake is not appropriate since relatively small amounts of time is spent in these microenvironments

## HEALTH CONCERNS

Nickel carbonyl appears to be the most acutely toxic nickel compound to both humans and animals. Immediate and delayed toxic effects have been associated with nickel carbonyl poisoning (ie. in occupational environments). The immediate symptomatology includes frontal headache, nausea, vomiting, insomnia and irritability. The delayed effects are pulmonary effects such as constrictive chest pains, dry coughing, dyspnoea, cyanosis, tachycardia, sweating and visual disturbances. Deaths have been associated with pulmonary haemorrhage, oedema or pneumonitis. Other organs affected include liver, kidney, spleen and the adrenals. In animals, the inhalation  $\text{LC}_{50}$  values (median lethal concentrations) range from  $0.067 \text{ mg/L}$  (mouse) to  $0.24 \text{ mg/L}$  (rats). The adverse effects of other nickel compounds are insignificant.

Effects of short and long term exposures to nickel compounds by workers in nickel industry include rhinitis, chronic rhinitis, pneumoconiosis and sinusitis (with apparent injuries such as nasal septal erosions, perforations and ulcerations). There are incidences of hypo-osmia and anosmia. Nephrotoxicity and cardiovascular toxicity have also been observed.

Reduced survival has been observed in rats treated chronically with nickel compounds at concentrations as low as  $60 \text{ ug/m}^3$ . Systemic adverse effects have been obtained in rats given nickel at concentrations as low as  $109 \text{ ug/m}^3$ .

Carcinogenicity appears to be a major concern for nickel and its compounds. Nickel compounds have been evaluated as class I carcinogens by the International Agency for Research on Cancer (IARC), indicating that these compounds are carcinogenic to humans. Metallic nickel has been classified as 2B, indicating that it may be a possible human carcinogen. The predominant cancer types are pulmonary, nasal and laryngeal cancers which are found with high frequency among nickel refinery and plating workers. The incidences of cancer among factory workers have been on the decline in recent years due to improvements in controlled nickel emission.

It should be noted that nickel compounds exhibit various interactions with other compounds. Nickel ions have been found to enhance the transformation frequency and mutagenicity of benzo[a]pyrene in animal cells. In other cases, nickel appears to antagonize the adverse effects of other metals such as copper.

Various health criteria (ie. Unit risks, Reference concentrations, ambient air quality guidelines) from lead agencies are summarized in Table 2. This table also includes the calculated "allowable" intake associated with the listed health criteria.

TABLE 2. Summary of Exposure Guidelines for Nickel from Leading Agencies

GUIDELINE APPLICATION	AGENCY(IES)	ORIGINAL VALUE	CONCENTRATION ("Original Form" converted to these -as applicable)			CALCULATED "ALLOWABLE" INTAKE (3)
			Unit Risk (1)	RsC (2) (1 x 10 <sup>-4</sup> )	RsC (2) (1 x 10 <sup>-5</sup> )	
INHALATION GUIDELINES						
Occupational	ACGIH, Ontario	50 - 1000 ug/m <sup>3</sup>	NA	NA	NA	1000 - 20000 (0.014 - 0.28)
Ambient Air Quality Guidelines	US states,	0.015 -0.18 ug/m <sup>3</sup>	NA	NA	NA	0.3 - 3.6 (4.3 x 10 <sup>-4</sup> - 5.1 x 10 <sup>-4</sup> )
Air Quality Guideline	Ontario	2 ug/m <sup>3</sup>	NA	NA	NA	40 (5.7 x 10 <sup>-4</sup> )
Chronic AELs/RfCs	CDHS WHO	0.24 ug/m <sup>3</sup> NA	NA	NA	NA	4.8 (6.8 x 10 <sup>-5</sup> ) NA
Inhalation Cancer Potency Factor	EPA CDHS WHO	See Unit Risk column	2.4 X 10 <sup>-4</sup> 2.6 x 10 <sup>-4</sup> 4 x 10 <sup>-4</sup>	0.042 0.038 0.025	0.0042 0.0038 0.0025	for 1 x 10 <sup>-4</sup> risk: 0.5 - 0.84 (7.1 x 10 <sup>-4</sup> - 1.2 x 10 <sup>-4</sup> ) for 1 x 10 <sup>-6</sup> risk: 0.05-0.084 (7.1 x 10 <sup>-7</sup> - 1.2 x 10 <sup>-7</sup> )

<sup>1</sup>For inhalation guidelines, unit risks are expressed as ( $\mu\text{g}/\text{m}^3$ )<sup>-1</sup><sup>2</sup>For inhalation guidelines, risk specific concentrations are expressed as  $\mu\text{g}/\text{m}^3$ <sup>3</sup>Intake was computed by assuming, where applicable, an adult weight of 70 kg, a breathing rate of 20  $\text{m}^3/\text{day}$ . In all cases 100% bioavailability of the intake was assumed.

## RISK CHARACTERIZATION AND PERSPECTIVES

From the brief exposure analysis and the available health criteria the following observations can be made:

### Health messages:

- 1) All exposures are less than the chronic acceptable exposure levels (ie. 4.8 ug/day) proposed by California (CDHS).
- 2) The most conservative exposure guidelines available are the potencies shown in Table 3. The carcinogenic risk associated with 'outdoor air quality' (ie. 100 % outdoor exposure) is between  $9.2 \times 10^{-7}$  and  $4.1 \times 10^{-6}$ . Similarly the risk associated with 'typical outdoor exposures' (ie. 3 hr) is between  $1.2 \times 10^{-7}$  and  $6.0 \times 10^{-7}$ . Similarly the range of risks associated with indoor air environments (ie. those in which extended periods of exposure are expected) is between  $2.4 \times 10^{-7}$  and  $8.0 \times 10^{-7}$ . The risks associated

Table 3. Range of Inhalation Cancer Risks Associated with Estimated Intakes (ie. for adult exposures only) of Nickel.

RANGE of INHALATION INTAKES			POTENCY (a)		RANGE of RISKS
Environment	Unit ug/day	Unit mg/kg/day	Agency	Unit (mg/kg-d) <sup>1</sup>	
OUTDOOR AIR QUALITY (Windsor)	0.08 - 0.2	$1.1 \times 10^{-4}$ $2.9 \times 10^{-4}$	EPA	0.84 (a)	$9.2 \times 10^{-7} - 2.4 \times 10^{-6}$
			CDHS	0.91 (a)	$1.0 \times 10^{-6} - 2.6 \times 10^{-6}$
			WHO	1.4 (a)	$1.5 \times 10^{-6} - 4.1 \times 10^{-6}$
			OVERALL RANGE OF RISKS: $9.2 \times 10^{-7} - 4.1 \times 10^{-6}$		
TYPICAL OUTDOOR EXPOSURE (ie.= 3 hr.)	0.01 - 0.03	$1.4 \times 10^{-7}$ $4.3 \times 10^{-7}$	EPA	0.84 (a)	$1.2 \times 10^{-7} - 3.6 \times 10^{-7}$
			CDHS	0.91 (a)	$1.3 \times 10^{-7} - 3.9 \times 10^{-7}$
			WHO	1.4 (a)	$2.0 \times 10^{-7} - 6.0 \times 10^{-7}$
			OVERALL RANGE OF RISKS: $1.2 \times 10^{-7} - 6.0 \times 10^{-7}$		
INDOOR AIR ENVIRONMENTS (Extended periods of exposure expected)	0.02 - 0.04	$2.9 \times 10^{-7} -$ $5.7 \times 10^{-7}$	EPA	0.84 (a)	$2.4 \times 10^{-7} - 4.8 \times 10^{-7}$
			CDHS	0.91 (a)	$2.6 \times 10^{-7} - 5.2 \times 10^{-7}$
			WHO	1.4 (a)	$4.1 \times 10^{-7} - 8.0 \times 10^{-7}$
			OVERALL RANGE OF RISKS: $2.4 \times 10^{-7} - 8.0 \times 10^{-7}$		

a. These are equivalent potency factors calculated from the unit risks proposed by the agencies listed; assumed adult weight of 70 kg and 20 m<sup>3</sup> per day.

with 'outdoor air quality' are highest and risks associated with indoor air environments (ie. those in which extended periods of exposure are expected) and 'typical outdoor exposures' are slightly less and approximately equal. It should be noted that this risk characterization (ie. using carcinogenic based limits) is based on an assumed lifetime exposure (ie. 24 hours, every day, for 70 years) and hence is a very conservative assumption.



3) Exposures associated with indoor environments (ie. those in which extended periods of exposure are expected) are slightly higher than those associated with typical outdoor air exposures (ie. 3 hr).

**Regulatory compliance messages:**

4) All exposures associated with outdoor air quality(ie. 100 % outdoor exposure) fall in the lower 6 % range of air quality guidelines of various jurisdictions. All exposures associated with typical outdoor exposures (ie. 3 hr) and exposures associated with indoor air environments (ie. those in which extended periods of exposure are expected) fall in the lower 1 % range of air quality guidelines of various jurisdictions. All exposures are less than the Ontario guideline.

5) All exposures are less than the range of occupational levels.

6) MOEE is presently reviewing the basis of the existing standard for nickel.

**Summary and recommendations:**

♦ All exposures are less than the range of chronic acceptable exposure levels. Therefore, the possibility of long-term health effects, other than cancer risk, is unlikely.

♦ Since the levels of inhalation risk are less than  $1 \times 10^{-5}$ , a level generally deemed to be negligible, it is not necessary to place a high priority on exposure reduction for nickel.

**REFERENCES**

1. Agency for Toxic Substances and Disease Registry, U.S. Public Health Service. Toxicological Profile for Nickel. December, 1988.
2. World Health Organization (WHO). Air Quality Guidelines for Europe. Copenhagen, WHO Regional Publications, 1988. European Series No. 23. pp. 285 - 296.





## APPENDIX 18

### RISK ANALYSIS FOR VINYL CHLORIDE



## VINYL CHLORIDE

### NATURE of the CHEMICAL, SOURCES, LEVELS in OUTDOOR and INDOOR AIR, and ESTIMATED INTAKES.

Vinyl chloride (ie. chloroethene) is a colourless vapour at room temperature and pressure, with a mild odour. It is widely used in the synthesis of polyvinyl chloride by the plastic-manufacturing industry. Minor uses of vinyl chloride include the production of furniture, automobile upholstery, wall coverings, housewares, and automotive parts. There are no known natural sources of this compound. Its main route of entry into the environment is from plastic-manufacturing industry emissions. Other sources include tobacco smoke and emissions from hazardous waste sites. Because of the emissions from plastic-manufacturing industries, ambient air concentrations are generally higher in urban areas, especially near these industries, than rural areas.

Average (ie. 'mean') and 90th percentile concentrations (or range of concentrations) of vinyl chloride in outdoor and indoor air are summarized in Table 1. Estimated adult intakes per day in units of ug/day, associated with these concentrations, are also included in Table 1.

**Table 1. Levels of Vinyl Chloride in Outdoor and Indoor Air in Windsor and, Estimated Intakes per day (in ug/day) Associated with these Environments.**

ENVIRONMENTS	Concentration Mean or Range of Means  ug/m <sup>3</sup>	Concentration 90th percentile (or Range of)  ug/m <sup>3</sup>	Estimated Adult Range of Intakes per day  ug/day
Outdoor Air Quality - Windsor (ie. 100 % outdoor exposure) (a)	0.62 (e)	NA	12.4 (a),(d)
Typical outdoor exposure (ie. ≈ 3hr) (b)	0.62 (e)	NA	1.6 (b)
INDOOR AIR ENVIRONMENTS (c) (EXTENDED periods of exposure expected) (e.g. Home, office)	Not detected	NA	NA
INDOOR AIR ENVIRONMENTS (c) (BRIEF periods of exposure expected) (e.g. Commuting, bingo halls, taverns)	Not detected	NA	NA

a) Based on 224, 24 hour average samples (Note that vinyl chloride was detected only 6 times). Intake is associated with the 'maximum' concentration in outdoor air. Therefore this result should be interpreted with care. It is to be noted that people are not exposed 24 hours to outdoor air. This estimation assumes 100 % exposure to outdoor air and is a measure of outdoor air quality per se and not of actual exposure.

b) Intake calculated from the 'maximum' concentration in outdoor air and assuming a 'typical' outdoor air exposure of ≈ 3 hr (ie. corresponding to breathing 2.5 m<sup>3</sup>/3hr for adults).

c) Vinyl chloride was not detected in any of the Windsor personal exposure & microenvironment samples.

d) Assuming an inhalation rate of 20 m<sup>3</sup>/day

e) This is a maximum value.

## HEALTH CONCERNS

Both short-term and long-term exposures to levels at or above 10 ppm (26,000 ug/m<sup>3</sup>) have been associated with numerous toxic effects in both animals and humans. These effects include damage to the following organs and systems: liver, lungs, kidneys, heart, bones, testes, eyes, skin, circulatory system, immune system, and nervous system<sup>1</sup>. However, these levels of vinyl chloride which cause adverse health effects are much higher than the concentrations measured in the environment.

The cancer causing potential of vinyl chloride has been examined in several epidemiological and animal studies. In humans, vinyl chloride has been shown to cause liver, brain, lung, and blood cancer; animals developed cancer of the liver, lung, mammary gland, skin, ear, blood, kidney, and nerve cell. The International Agency for Research on Cancer ranks vinyl chloride as a human carcinogen.

Various health criteria (ie. Unit risks, Reference concentrations, ambient air quality guidelines) from lead agencies are summarized in Table 2. The table also includes the calculated "allowable" intake associated with the listed health criteria.

## RISK CHARACTERIZATION AND PERSPECTIVES

From the brief exposure analysis and the available health criteria the following observations can be made:

### Health messages:

- 1) All exposures are less than the chronic acceptable exposure levels (ie. 520 ug/day) proposed by California (CDHS).
- 2) The most conservative exposure guidelines available are the potencies shown in Table 3. The carcinogenic risk associated with 'outdoor air quality' (ie. 100 % outdoor exposure) is between  $6.3 \times 10^{-7}$  and  $4.9 \times 10^{-5}$ . Similarly the risk associated with 'typical outdoor exposures' (ie. 3 hr) is between  $8.1 \times 10^{-8}$  and  $6.2 \times 10^{-6}$ . The risks associated with 'outdoor air quality' are slightly higher than the risks associated with 'typical outdoor exposures'. These risk estimates should be interpreted with utmost care since they are based on maximum values in 6 samples, while 218 samples showed no detectable levels of vinyl chloride. If the risk estimates were based on the detection limit, they would be reduced by at least 6-fold, but could be even lower. It should be noted that this risk characterization (ie. using carcinogenic based limits) is based on an assumed lifetime exposure (ie. 24 hours, every day, for 70 years) and hence is a very conservative assumption.

### Regulatory compliance messages:

- 3) All exposures associated with outdoor air quality (ie. 100 % outdoor exposure) and typical outdoor exposure (ie. 3 hr) fall in the lower 5 % range of air quality guidelines of various jurisdictions. Exposures in indoor air environments are expected to be much lower (ie. vinyl chloride was not detected in indoor air). All exposures are less than the Ontario guideline.
- 4) All exposures are less than the range of occupational levels.



Table 2. Summary of Exposure Guidelines for Vinyl chloride from Leading Agencies

GUIDELINE APPLICATION	AGENCY(IES)	ORIGINAL VALUE	CONCENTRATION ("Original Form" converted to these as applicable)			CALCULATED "ALLOWABLE" INTAKE (3)
			Unit Risk (1)	RsC (2) (1 x 10 <sup>-3</sup> )	RsC (2) (1 x 10 <sup>-4</sup> )	
INHALATION GUIDELINES						
Occupational	ACGIH, Ontario	13000, NA ug/m <sup>3</sup>	NA	NA	NA	260000, NA (3.7, NA)
Ambient Air Quality Guidelines	US states,	0.02 - 13 ug/m <sup>3</sup>	NA	NA	NA	0.4 - 260 (5.7 x 10 <sup>-4</sup> - 3.7 x 10 <sup>-3</sup> )
Air Quality Guideline	Ontario	1 ug/m <sup>3</sup>	NA	NA	NA	20 (2.8 x 10 <sup>-4</sup> )
Chronic AELs/RfCs	CDHS WHO	26 ug/m <sup>3</sup> NA	NA	NA	NA	520 (7.4 x 10 <sup>-3</sup> )
Inhalation Cancer Potency Factor	EPA CDHS WHO	See Unit Risk column	NA 7.8 x 10 <sup>-4</sup> 1 x 10 <sup>-4</sup>	NA 0.13 10	NA 0.013 1	for 1 x 10 <sup>-4</sup> risk: 2.6 - 200 (3.7 x 10 <sup>-4</sup> - 2.8 x 10 <sup>-3</sup> ) for 1 x 10 <sup>-4</sup> risk: 0.26 - 20 (3.7 x 10 <sup>-4</sup> - 2.8 x 10 <sup>-3</sup> )

<sup>1</sup>For inhalation guidelines, unit risks are expressed as (ug/m<sup>3</sup>)<sup>-1</sup>

<sup>2</sup>For inhalation guidelines, risk specific concentrations are expressed as ug/m<sup>3</sup>

<sup>3</sup>Intake was computed by assuming, where applicable, an adult weight of 70 kg, a breathing rate of 20 m<sup>3</sup>/day. In all cases 100% bioavailability of the intake was assumed.

Table 3. Range of Inhalation Cancer Risks Associated with Estimated Intakes (ie. for adult exposures only) of Vinyl Chloride.

RANGE of INHALATION INTAKES			POTENCY (a)		RANGE of RISKS
Environment	Unit ug/day	Unit mg/kg/day	Agency	Unit (mg/kg-d) <sup>a</sup>	
OUTDOOR AIR QUALITY (Windsor)	12.4	1.8 x 10 <sup>-4</sup>	EPA	N.A.	
			CDHS	0.27 (a)	4.9 x 10 <sup>-5</sup>
			WHO	0.0035	6.3 x 10 <sup>-7</sup>
			OVERALL RANGE OF RISKS: 6.3 x 10 <sup>-7</sup> - 4.9 x 10 <sup>-5</sup>		
TYPICAL OUTDOOR EXPOSURE (ie.= 3 hr.)	1.6	2.3 x 10 <sup>-5</sup>	EPA	N.A.	
			CDHS	0.27 (a)	6.2 x 10 <sup>-4</sup>
			WHO	0.0035	8.1 x 10 <sup>-4</sup>
			OVERALL RANGE OF RISKS: 8.1 x 10 <sup>-4</sup> - 6.2 x 10 <sup>-4</sup>		
INDOOR AIR ENVIRONMENTS (Extended periods of exposure expected)	Not Detec ted	NA	EPA	N.A.	NA
			CDHS	0.27 (a)	NA
			WHO	0.0035	NA
			OVERALL RANGE OF RISKS: NA		
a. These are equivalent potency factors calculated from the unit risks proposed by the agencies listed; assumed adult weight of 70 kg and 20 m <sup>3</sup> per day.					

#### Summary and recommendations:

- ♦ All exposures are less than the range of chronic acceptable exposure levels. Therefore, the possibility of long-term health effects, other than cancer risk, is unlikely.
- ♦ Since the levels of inhalation risk are likely less than  $1 \times 10^{-5}$ , a level generally deemed to be negligible, it is not necessary to place a high priority on exposure reduction for vinyl chloride.

#### REFERENCES

1. Agency for Toxic Substances and Disease Registry, U.S. Public Health Service. Toxicological Profile for Vinyl chloride. October 1991.

**APPENDIX 19**

**RISK ANALYSIS FOR BERYLLIUM**



## BERYLLIUM

### NATURE of the CHEMICAL, SOURCES, LEVELS in OUTDOOR and INDOOR AIR, and ESTIMATED INTAKES.

Beryllium, in a pure form, is a hard grayish metal. It is widely used in the manufacture of electronic devices, structural components of aircraft, satellites, parts of nuclear reactors and X-ray machines, nuclear weapons, mirrors, and specialty ceramics. Beryllium is present in nature as a component of specific types of rocks and soil. It is released to the environment from both biogenic and anthropogenic sources, however, the latter is the primary contributor. The biogenic sources include windblown dusts and volcanoes; the anthropogenic sources include the burning of coal or fuel oil, tobacco smoke, and industries that are involved in processing beryllium ore, metal fabrication, and production and use of beryllium oxide. Because of this, ambient air concentrations are generally higher in urban areas than rural.

Average (ie. 'mean') and 90th percentile concentrations (or range of concentrations) of beryllium in outdoor and indoor air are summarized in Table 1. Estimated adult intakes per day in units of ug/day, associated with these concentrations, are also included in Table 1.

**Table 1. Levels of Beryllium in Outdoor and Indoor Air in Windsor and, Estimated Intakes per day (in ug/day) Associated with these Environments.**

ENVIRONMENTS	Concentration Mean or Range of Means  ug/m <sup>3</sup>	Concentration 90th percentile (or Range of)  ug/m <sup>3</sup>	Estimated Adult Range of Intakes per day  ug/day
Outdoor Air Quality - Windsor (ie. 100 % outdoor exposure) (a)	$9 \times 10^{-5} - 1.4 \times 10^{-4}$	NA	$1.8 \times 10^{-3} - 2.8 \times 10^{-3}$ (a),(d)
Typical outdoor exposure (ie. $\approx$ 3hr) (b)	$9 \times 10^{-5} - 1.4 \times 10^{-4}$	NA	$2.3 \times 10^{-4} - 3.5 \times 10^{-4}$ (b)
INDOOR AIR ENVIRONMENTS (c) (EXTENDED periods of exposure expected) (e.g. Home, office)	Not detected	NA	NA
INDOOR AIR ENVIRONMENTS (c) (BRIEF periods of exposure expected) (e.g. Commuting, bingo halls, taverns)	Not detected	NA	NA

a) Based on 55, 24 hour average samples (The range of values represent the range of maximum values from two sites). Range of intakes is associated with the range of the 'maximum' concentrations in outdoor air. It is to be noted that people are not exposed 24 hours to outdoor air. This estimation assumes 100 % exposure to outdoor air and is a measure of outdoor air quality per se and not of actual exposure.

b) Range of intakes calculated from the 'maximum' concentrations in outdoor air and assuming a 'typical' outdoor air exposure of  $\approx$  3 hr (ie. corresponding to breathing 2.5 m<sup>3</sup>/3hr for adults).

c) Beryllium was not detected in any of the Windsor personal exposure & microenvironment samples.

d) Assuming an inhalation rate of 20 m<sup>3</sup>/day



## HEALTH CONCERNS

Both short-term and long-term exposures to levels at or above 34 ug/m<sup>3</sup> beryllium have been associated with toxic effects in both animals and humans. The major effect caused by beryllium is lung damage<sup>1</sup>. However, these levels of beryllium which cause adverse health effects are much higher than the concentrations measured in the environment.

The cancer causing potential of beryllium has been examined in several epidemiological and animal studies. It has been shown to cause lung tumors in rats. The U.S.EPA ranks beryllium as a probable human carcinogen.

Various health criteria (ie. Unit risks, Reference concentrations, ambient air quality guidelines) from lead agencies are summarized in Table 2. The table also includes the calculated "allowable" intake associated with the listed health criteria.

## RISK CHARACTERIZATION AND PERSPECTIVES

From the brief exposure analysis and the available health criteria the following observations can be made:

### Health messages:

- 1) All exposures are less than the chronic acceptable exposure level (ie.  $9.6 \times 10^{-2}$  ug/day) proposed by California (CDHS).
- 2) The most conservative exposure guidelines available are the potencies shown in Table 3. The carcinogenic risk associated with 'outdoor air quality' (ie. 100 % outdoor exposure) is between  $2.2 \times 10^{-7}$  and  $3.4 \times 10^{-7}$ . Similarly the risk associated with 'typical outdoor exposures' (ie. 3 hr) is between  $2.2 \times 10^{-8}$  and  $4.2 \times 10^{-8}$ . The risks associated with 'outdoor air quality' are slightly higher than the risks associated with 'typical outdoor exposures'. It should be noted that this risk characterization (ie. using carcinogenic based limits) is based on an assumed lifetime exposure (ie. 24 hours, every day, for 70 years) and hence is a very conservative assumption.

### Regulatory compliance messages:

- 3) All exposures associated with outdoor air quality (ie. 100 % outdoor exposure) and typical outdoor exposure (ie. 3 hr) fall in the lower 35 % range of air quality guidelines of various jurisdictions. Exposures associated with indoor air environments (ie. those in which extended periods of exposure are expected) are expected to be much lower (ie. Beryllium was not detected in indoor air). All exposures are less than the Ontario guideline.
- 4) All exposures are less than the range of occupational levels.

Table 2. Summary of Exposure Guidelines for Beryllium from Leading Agencies

GUIDELINE APPLICATION	AGENCY(IES)	ORIGINAL VALUE	CONCENTRATION ("Original Form" converted to these -as applicable)			CALCULATED "ALLOWABLE" INTAKE (3)
			Unit Risk (1)	R <sub>SC</sub> (2) (1 x 10 <sup>-5</sup> )	R <sub>SC</sub> (2) (1 x 10 <sup>-6</sup> )	
				ug/day (mg/kg/day)		
INHALATION GUIDELINES						
Occupational	ACGIH, Ontario	2 ug/m <sup>3</sup>	NA	NA	NA	40 (5.7 x 10 <sup>-4</sup> )
Ambient Air Quality Guidelines	US states,	4.1 x 10 <sup>-4</sup> - 4 x 10 <sup>-4</sup> ug/m <sup>3</sup>	NA	NA	NA	8.2 x 10 <sup>-5</sup> - 0.008 (1.2 x 10 <sup>-5</sup> - 1.1 x 10 <sup>-7</sup> )
Air Quality Guideline	Ontario	0.01 ug/m <sup>3</sup>	NA	NA	NA	0.2 (2.8 x 10 <sup>-4</sup> )
Chronic AELs/RfCs	CDHS WHO	0.0048 ug/m <sup>3</sup> NA	NA	NA	NA	0.096 (1.4 x 10 <sup>-6</sup> ) NA
Inhalation Cancer Potency Factor	EPA CDHS WHO	See Unit Risk column	2.4 x 10 <sup>-3</sup> 2.4 x 10 <sup>-3</sup> NA	0.004 0.004 NA	0.0004 0.0004 NA	for 1 x 10 <sup>-4</sup> risk: 0.08 (1.1 x 10 <sup>-4</sup> ) for 1 x 10 <sup>-6</sup> risk: 0.008 (1.1 x 10 <sup>-7</sup> )

<sup>1</sup>For inhalation guidelines, unit risks are expressed as (ug/m<sup>3</sup>)<sup>-1</sup>

<sup>2</sup>For inhalation guidelines, risk specific concentrations are expressed as ug/m<sup>3</sup>

<sup>3</sup>Intake was computed by assuming, where applicable, an adult weight of 70 kg, a breathing rate of 20 m<sup>3</sup>/day. In all cases 100% bioavailability of the intake was assumed.

Table 3. Range of Inhalation Cancer Risks Associated with Estimated Intakes (ie. for adult exposures only) of Beryllium

RANGE of INHALATION INTAKES			POTENCY (a)		RANGE of RISKS
Environment	Unit ug/day	Unit mg/kg/day	Agency	Unit (mg/kg-d) <sup>a</sup>	
OUTDOOR AIR QUALITY (Windsor)	1.8 x 10 <sup>-3</sup> - 2.8 x 10 <sup>-3</sup>	2.6 x 10 <sup>-4</sup> 4 x 10 <sup>-4</sup>	EPA	8.4 (a)	2.2 x 10 <sup>-7</sup> - 3.4 x 10 <sup>-7</sup>
			CDHS	8.4 (a)	Same as above
			WHO	None proposed	NA
			OVERALL RANGE OF RISKS: 2.2 x 10 <sup>-7</sup> - 3.4 x 10 <sup>-7</sup>		
TYPICAL OUTDOOR EXPOSURE (ie.= 3 hr.)	2.3 x 10 <sup>-4</sup> - 3.5 x 10 <sup>-4</sup>	3.3 x 10 <sup>-4</sup> 5.0 x 10 <sup>-4</sup>	EPA	8.4 (a)	2.8 x 10 <sup>-4</sup> - 4.2 x 10 <sup>-4</sup>
			CDHS	8.4 (a)	Same as above
			WHO	None proposed	
			OVERALL RANGE OF RISKS: 2.2 x 10 <sup>-4</sup> - 4.2 x 10 <sup>-4</sup>		
INDOOR AIR ENVIRONMENTS (Extended periods of exposure expected)	NA	NA	EPA	8.4 (a)	NA
			CDHS	8.4 (a)	Same as above
			WHO	None proposed	
			OVERALL RANGE OF RISKS: NA		

a. These are equivalent potency factors calculated from the unit risks proposed by the agencies listed; assumed adult weight of 70 kg and 20 m<sup>3</sup> per day.

#### Summary and recommendations:

- ♦ All exposures are less than the range of chronic acceptable exposure levels. Therefore, the possibility of long-term health effects, other than cancer risk, is unlikely.
- ♦ Since the levels of inhalation risk are less than  $1 \times 10^{-3}$ , a level generally deemed to be negligible, it is not necessary to place a high priority on exposure reduction for beryllium.

#### REFERENCES

1. Agency for Toxic Substances and Disease Registry, U.S. Public Health Service. Toxicological Profile for Beryllium. December 1988.

## APPENDIX 20

### RISK ANALYSIS FOR ACETALDEHYDE





## ACETALDEHYDE

### NATURE of the CHEMICAL, SOURCES, LEVELS in OUTDOOR and INDOOR AIR, and ESTIMATED INTAKES.

Acetaldehyde (i.e. acetic aldehyde) is a colourless, volatile, inflammable liquid at room temperature and pressure with a strong odour. It is widely used as a chemical intermediate in the synthesis of other chemicals, perfumes, polyester resins, and dyes; as a food preservative and flavouring agent; as a solvent in the rubber, tanning, and paper industries; and in fuel. Acetaldehyde is formed in nature. It is released into the environment from both biogenic and anthropogenic sources. The biogenic sources include plants which produce acetaldehyde during respiration; the anthropogenic sources include the incomplete combustion of wood residential fireplaces and woodstoves, vehicle exhaust, tobacco smoke, emissions from industries that produce or use acetaldehyde, and in situ synthesis from photooxidation of hydrocarbons in photochemical smog. Because of this, ambient air concentrations are generally higher in urban areas than rural.

Average (ie. 'mean') and 90th percentile concentrations (or range of concentrations) of acetaldehyde in outdoor and indoor air are summarized in Table 1. Estimated adult intakes per day in units of ug/day, associated with these concentrations, are also included in Table 1.

**Table 1. Levels of Acetaldehyde in Outdoor and Indoor Air in Windsor and, Estimated Intakes per day (in ug/day) Associated with these Environments.**

ENVIRONMENTS	Concentration Mean or Range of Means  ug/m <sup>3</sup>	Concentration 90th percentile (or Range of)  ug/m <sup>3</sup>	Estimated Adult Range of Intakes per day  ug/day
Outdoor Air Quality - Windsor (ie. 100 % outdoor exposure) (a)	1.4 - 3.6	2.3 - 5.0	28 - 100 (a),(d)
Typical outdoor exposure (ie. ~ 3hr) (b)	1.4 - 3.6	2.3 - 5.0	3.5 - 12.5 (b)
INDOOR AIR ENVIRONMENTS (c) (EXTENDED periods of exposure expected) (e.g. Home, office)	7.5 - 21.5	17.5 - 44.1	131 - 772 (e)
INDOOR AIR ENVIRONMENTS (c) (BRIEF periods of exposure expected) (e.g. Commuting, bingo halls, taverns)	42	76 (maximum value)	Not included (f)

- a) Based on 224, 24 hour average samples. Range of intakes is associated with the range of the lowest 'mean' to the highest '90th percentile' concentrations in outdoor air. It is to be noted that people are not exposed 24 hours to outdoor air. This estimation assumes 100 % exposure to outdoor air and is a measure of outdoor air quality per se and not of actual exposure.
- b) Range of intakes calculated from the lowest 'mean' to the highest '90th percentile' concentrations in outdoor air and assuming a 'typical' outdoor air exposure of  $\approx 3$  hr (ie. corresponding to breathing  $2.5 \text{ m}^3/\text{hr}$  for adults).
- c) From the Windsor personal exposure & microenvironment studies
- d) Assuming an inhalation rate of  $20 \text{ m}^3/\text{day}$
- e) Range of intakes is estimated from the range of the lowest 'mean' and the highest '90th percentile' concentrations obtained from personal exposure and microenvironment measurements in indoor environments in environments where extended periods of exposure are expected. A total exposure of 21 hours (ie.  $17.5 \text{ m}^3/\text{day}$ ) was assumed for these indoor environments.
- f) Direct estimation of daily intake is not appropriate since relatively small amounts of time is spent in these microenvironments

## HEALTH CONCERNS

Both short-term and long-term exposures have been associated with toxic effects in both animals and humans. These effects include irritation of the eyes, skin, and respiratory tract, respiration rate decrease, blood pressure increase, pulmonary edema, and narcosis. The acetaldehyde concentration at which no adverse health effects were observed could not be determined due to the poor quality of the studies.

The cancer causing potential of acetaldehyde has been examined in several animal studies. It has been shown to cause tumors of the respiratory tract in rats and hamsters. U.S.EPA ranks acetaldehyde as a probable human carcinogen.

Various health criteria (ie. Unit risks, Reference concentrations, ambient air quality guidelines) from lead agencies are summarized in Table 2. The table also includes the calculated "allowable" intake associated with the listed health criteria.

## RISK CHARACTERIZATION AND PERSPECTIVES

From the brief exposure analysis and the available health criteria the following observations can be made:

### Health messages:

- 1) All exposures, except the higher end of indoor environments (ie. those in which extended periods of exposure are expected), are less than the chronic acceptable exposure level (ie.  $180 \text{ ug}/\text{day}$ ) proposed by California (CDHS).
- 2) The most conservative exposure guidelines available are the potencies shown in Table 3. The carcinogenic risk associated with 'outdoor air quality' (ie. 100 % outdoor exposure) is between  $3.1 \times 10^{-6}$  and  $1.3 \times 10^{-5}$ . Similarly the risk associated with 'typical outdoor exposures' (ie. 3 hr) is between  $3.9 \times 10^{-7}$  and  $1.7 \times 10^{-6}$ . Similarly the range of risks associated with indoor air environments (ie. those in which extended periods of exposure are expected) is between  $1.5 \times 10^{-5}$  and  $1.0 \times 10^{-4}$ . The risks associated with indoor air environments (ie. those in which extended periods of exposure are expected) are slightly higher than the risks associated with 'outdoor air quality' which in turn is higher than 'typical outdoor exposures'. It should be noted that this risk characterization (ie. using carcinogenic based limits) is based on an assumed lifetime exposure (ie. 24 hours, every day, for 70 years) and hence is a very conservative assumption.

Table 2. Summary of Exposure Guidelines for Acetaldehyde from Leading Agencies

GUIDELINE APPLICATION	AGENCY(IES)	ORIGINAL VALUE	CONCENTRATION ("Original Form" converted to these -as applicable)			CALCULATED "ALLOWABLE" INTAKE (3)
			Unit Risk (1)	R <sub>50</sub> (2) (1 x 10 <sup>-4</sup> )	R <sub>50</sub> (2) (1 x 10 <sup>-5</sup> )	
INHALATION GUIDELINES						
Occupational	ACGIH, Ontario	45000 - 180000 ug/m <sup>3</sup>	NA	NA	NA	900000 - 3600000 (12.8 - 51.4)
Ambient Air Quality Guidelines	US states,	0.4 -430 ug/m <sup>3</sup>	NA	NA	NA	8 - 8600 (1.1 x 10 <sup>-4</sup> - 0.12)
Air Quality Guideline	Ontario	NA	NA	NA	NA	NA
Chronic AELs/RfCs	CDHS US EPA	9 ug/m <sup>3</sup>	NA	NA	NA	180 (2.6 x 10 <sup>-3</sup> )
Inhalation Cancer Potency Factor	EPA CDHS WHO	See Unit Risk column	2.2 x 10 <sup>-4</sup> 2.7 x 10 <sup>-4</sup> NA	5 3.7 NA	0.5 0.37 NA	for 1 x 10 <sup>-4</sup> risk: 74 - 100 (1.1 x 10 <sup>-3</sup> - 1.4 x 10 <sup>-3</sup> ) for 1 x 10 <sup>-5</sup> risk:7.4 - 10 (1.1 x 10 <sup>-4</sup> - 1.4 x 10 <sup>-4</sup> )

<sup>1</sup>For inhalation guidelines, unit risks are expressed as (ug/m<sup>3</sup>)<sup>-1</sup>

<sup>2</sup>For inhalation guidelines, risk specific concentrations are expressed as ug/m<sup>3</sup>

<sup>3</sup>Intake was computed by assuming, where applicable, an adult weight of 70 kg, a breathing rate of 20 m<sup>3</sup>/day, In all cases 100% bioavailability of the intake was assumed.

3) Exposures associated with indoor environments (ie. those in which extended periods of exposure are expected) exceed those associated with typical outdoor air exposures (ie. 3 hr).

#### Regulatory compliance messages:

4) All exposures associated with outdoor air quality(ie. 100 % outdoor exposure) and typical outdoor exposure (ie. 3 hr) fall in the lower 1 % range of air quality guidelines of various jurisdictions. Exposures associated with indoor air environments (ie. those in which extended periods of exposure are expected) fall in the lower 10 % range of air quality guidelines of various jurisdictions. An air quality guideline has not been set in Ontario.

5) All exposures are less than the range of occupational levels.

Table 3. Range of Inhalation Cancer Risks Associated with Estimated Intakes(ie. for adult exposures only) of Acetaldehyde

RANGE of INHALATION INTAKES			POTENCY (a)		RANGE of RISKS
Environment	Unit ug/day	Unit mg/kg/day	Agency	Unit (mg/kg-d) <sup>1</sup>	
OUTDOOR AIR QUALITY (Windsor)	28 - 100	4.0 x 10 <sup>-4</sup> 1.4 x 10 <sup>-3</sup>	EPA	0.0077 (a)	3.1 x 10 <sup>-4</sup> - 1.1 x 10 <sup>-5</sup>
			CDHS	0.0094 (a)	3.8 x 10 <sup>-4</sup> - 1.3 x 10 <sup>-5</sup>
			WHO	None proposed	
			OVERALL RANGE OF RISKS: 3.1 x 10 <sup>-4</sup> - 1.3 x 10 <sup>-5</sup>		
TYPICAL OUTDOOR EXPOSURE (ic. 3 hr.)	3.5 - 12.5	5.0 x 10 <sup>-5</sup> 1.8 x 10 <sup>-4</sup>	EPA	0.0077 (a)	3.9 x 10 <sup>-7</sup> - 1.4 x 10 <sup>-4</sup>
			CDHS	0.0094 (a)	4.7 x 10 <sup>-7</sup> - 1.7 x 10 <sup>-4</sup>
			WHO	None proposed	
			OVERALL RANGE OF RISKS: 3.9 x 10 <sup>-7</sup> - 1.7 x 10 <sup>-4</sup>		
INDOOR AIR ENVIRONMENTS (Extended periods of exposure expected)	131 - 772	1.9 x 10 <sup>-3</sup> - 1.1 x 10 <sup>-2</sup>	EPA	0.0077 (a)	1.5 x 10 <sup>-5</sup> - 8.5 x 10 <sup>-5</sup>
			CDHS	0.0094(a)	1.8 x 10 <sup>-5</sup> - 1.0 x 10 <sup>-4</sup>
			WHO	None proposed	
			OVERALL RANGE OF RISKS: 1.5 x 10 <sup>-5</sup> - 1.0 x 10 <sup>-4</sup>		

a. These are equivalent potency factors calculated from the unit risks proposed by the agencies listed; assumed adult weight of 70 kg and 20 m<sup>3</sup> per day.

### Summary and recommendations:

♦ All exposures, except the higher end of indoor environments (ie. those in which extended periods of exposure are expected), are less than the range of chronic acceptable exposure levels. Therefore, the possibility of long-term health effects, other than cancer risk, are possible in these indoor environments. It is recommended that these indoor environments should be a high priority for exposure reduction.

♦ Since the levels of inhalation risk are less than  $1 \times 10^{-5}$  (ie. except in indoor environments), a level generally deemed to be negligible, it is recommended that acetaldehyde be considered a candidate for exposure reduction in these environments.

### REFERENCES

1. Environmental Criteria and Assessment Office. U.S.EPA. Health Assessment Document for Acetaldehyde (Draft). June 1986.





**APPENDIX 21**  
**RISK ANALYSIS FOR LEAD**



## LEAD

### NATURE of the CHEMICAL, SOURCES, LEVELS in OUTDOOR and INDOOR AIR, and ESTIMATED INTAKES.

Lead is a toxic heavy metal which has had widespread historical use. At one time, lead was contained in a number of products including: solder used in cans and plumbing, gasoline, paints and certain pesticides. The past several decades have demonstrated a marked reduction in lead exposure for the general population. This reduction can largely be attributed to the phase-out of leaded gasoline. However, while exposure to lead has greatly diminished, several recent studies on the health effects of lead suggest adverse effects can occur at levels of exposure previously considered safe.

Average (ie. 'mean') and 90th percentile concentrations (or range of concentrations) of lead in outdoor and indoor air are summarized in Table 1. Estimated child intakes per day in units of ug/day (see section on 'Health Concerns' for the reasons why the focus is on children), associated with these concentrations, are also included in Table 1.

**Table 1. Levels of Lead in Outdoor and Indoor Air in Windsor and, Estimated Intakes per day (in ug/day) Associated with these Environments.**

ENVIRONMENTS	Concentration Mean or Range of Means  ug/m <sup>3</sup>	Concentration 90th percentile (or Range of)  ug/m <sup>3</sup>	Estimated Child Range of Intakes per day  ug/day
Outdoor Air Quality - Windsor (ie. 100 % outdoor exposure) (a)	0.04	0.08	0.2 - 0.4 (a),(d)
Typical outdoor exposure (ie. ~ 3hr) (b)	0.04	0.08	0.03 - 0.05 (b)
INDOOR AIR ENVIRONMENTS (c) (EXTENDED periods of exposure expected) (e.g. Home, office)	0.008 - 0.01	0.02 - 0.05	0.04 - 0.22 (e)
INDOOR AIR ENVIRONMENTS (c) (BRIEF periods of exposure expected) (e.g. Commuting, bingo halls, taverns)	0.01	0.02 (g)	Not included (f)

a) Based on 3181, 24 hour average samples. Range of intakes is associated with the range of the 'mean' to the '90th percentile' concentrations in outdoor air. It is to be noted that people are not exposed 24 hours to outdoor air. This estimation assumes 100 % exposure to outdoor air and is a measure of outdoor air quality per se and not of actual exposure.

b) Range of intakes calculated from the 'mean' to '90th percentile' concentrations in outdoor air and assuming a 'typical' outdoor air exposure of ~ 3 hr (ie. corresponding to breathing 0.63 m<sup>3</sup>/3hr for children).

c) From the Windsor personal exposure & microenvironment studies.

d) Assuming an inhalation rate of 5 m<sup>3</sup>/day (equivalent to a child).

e) Range of intakes is estimated from the range of the lowest 'mean' and the highest '90th percentile' concentrations obtained from personal exposure and microenvironmental measurements in indoor environments where extended periods of exposure are expected. A total exposure of 21 hours (ie. 4.4 m<sup>3</sup>/day for a child) was assumed for these indoor environments.

f) Direct estimation of daily intake is not appropriate since relatively small amounts of time is spent in these environments.

g) This is a maximum value.

## HEALTH CONCERNS

The effects of lead on human health are varied. Exposure to lead can adversely affect many organ systems including the reproductive, renal, cardio-vascular, blood forming and developing central nervous systems. Young children (aged six months to 4 years) are considered at greater risk of lead exposure due to the fact that they absorb lead more efficiently than adults and, on a body weight basis, they have a greater daily intake. Several studies which have examined the relationship between blood lead levels (as an indicator of exposure) in children have suggested that behavioural effects and learning deficits can occur at levels as low as 10 µg/dL; levels previously regarded as safe. It is also possible however, that adverse health effects may occur at blood lead levels below 10 µg/dL. Based on these studies, many jurisdictions including the MOEE recognize a blood lead level of 10 µg/dL as a blood lead level of concern.

It should be noted that lead has been reported to be an animal carcinogen with many independent studies reporting high incidence of distinctive kidney tumours in rodents exposed to high doses of lead. Carcinogenicity, however, is not considered the most critical endpoint as the rodent tumours occurred at exposure levels much higher than those which give rise to learning and behavioural deficits in children.

In a recent initiative, which established the basis for proposing revised environmental standards and guidelines for drinking water, air and soil, the MOEE recommended the use of an Intake of Concern (IOCpop) of 1.85 µg/kg/day for lead (MOEE 1993a). The IOCpop was derived by determining the daily intake in children which roughly corresponds to a blood lead level of 10 µg/dl (3.7 µg/kg/day) and applying a factor of 2 to account for variability in the population and uncertainty. The IOCpop corresponds to a daily intake of approximately 23.4 µg/day for children. Recent estimates suggest that the daily intake for urban children in Ontario is very close to 25 µg/day (MOEE 1993a).



Table 2: International Guidelines for Lead Levels in Air:

AGENCY	LIMIT	COMMENTS
CANADIAN PROVINCES		
Ontario (existing)	5 µg/m <sup>3</sup> 3 µg/m <sup>3</sup>	24 hour exposure period guideline 30 day mean
Ontario (proposed)	2 µg/m <sup>3</sup> 0.7 µg/m <sup>3</sup>	24 hour exposure period guideline 30 day mean
Manitoba	5 µg/m <sup>3</sup>	24 hour exposure period guideline
Quebec	0.2 µg/m <sup>3</sup>	annual exposure period guideline
Newfoundland	5 µg/m <sup>3</sup>	24 hour exposure period guideline
	2 µg/m <sup>3</sup>	30 day exposure period guideline
Montreal Urban Community	10 µg/m <sup>3</sup>	1 hour exposure period guideline
	5 µg/m <sup>3</sup>	8 hour exposure period guideline
British Columbia	1-2.5 µg/m <sup>3</sup>	an objective based on ecological, health, technological and economic considerations
Ambient air control objectives (1979)	4 µg/m <sup>3</sup>	24 hour maximum desirable level (guideline) based on ecological, health, technological and economic considerations
Ambient air quality guidelines	4 µg/m <sup>3</sup>	24 hour maximum acceptable level (guideline)
	6 µg/m <sup>3</sup>	24 hour maximum tolerable level (guideline)
UNITED STATES		
OAQPS: national ambient air quality standards	1.5 µg/m <sup>3</sup>	maximum arithmetic mean over calendar quarter based on human health effects (standard)
Selected State Acceptable Ambient Air Limits		
California	1.5 µg/m <sup>3</sup>	30 day arithmetic mean (standard)
Connecticut	3.0 µg/m <sup>3</sup>	8-hour average (guideline)
Kansas	0.357 µg/m <sup>3</sup>	1-year average (guideline)
Massachusetts	0.140 µg/m <sup>3</sup> 0.070 µg/m <sup>3</sup>	24-hour average (guideline) annual average (guideline)
European Community	2 µg/m <sup>3</sup>	maximum limit
Germany	0.1 mg/m <sup>3</sup>	8 hr TWA
WHO	30-60 µg/m <sup>3</sup>	maximum limit

## RISK CHARACTERIZATION AND PERSPECTIVES

Air quality standards and guidelines used by a variety of agencies are provided in Table 2. These limits are based both on health considerations as well as considerations of technical achievability and cost. The air monitoring data presented in Table 1 is well within these guidelines.

Exposure to lead comes from many sources including: soil, drinking water, consumer products, lead-based paints and air. Of the many pathways involved, direct inhalation from air represents less than 1% of a child's total exposure to lead. Therefore, while air monitoring data for lead would indicate that the levels of lead in ambient air are not a particular concern for the area, an assessment of overall risk can only be made by examining all routes of exposure. Additional information on lead and means of reducing exposure can be found in the document entitled "Rationale for the Development of Soil, Drinking Water, and Air Quality Criteria for Lead" (MOEE, 1993b).

## REFERENCES

1. MOEE 1993a, "Scientific Criteria Document for Multimedia Standards Development: Lead"; Authors, S. Fleming and F. Grilli (in press).
2. MOEE 1993b, "Rationale for the Development of Soil, Drinking Water and Air Quality Criteria for Lead" (in press)

**APPENDIX 22**

**RISK ANALYSIS FOR INORGANIC ARSENIC**



## INORGANIC ARSENIC

### NATURE OF THE CHEMICAL, SOURCES, LEVELS IN OUTDOOR AND INDOOR AIR, AND ESTIMATED INTAKES.

Arsenic generally exists in nature as a compound, not as the metal, with valence states of +3 (arsenite) and +5 (arsenate). Its main use is as a wood preservative (chromated copper arsenate). It is also used in the glass industry and in electronics (semiconductors) and as feed additives (organic arsenicals).

The primary anthropogenic sources to the atmosphere of inorganic arsenic in Ontario are copper and nickel smelters, iron ore sintering and coal burning power plants. The major natural source is forest fires. Although arsenic volatilizes during combustion, it condenses out on other particles and is emitted and transported in particulate form. The highest concentrations are usually found on the smallest particles. The median concentration in urban areas in Ontario is 1-4 ng/m<sup>3</sup>, although maximum values of up to 200 ng/m<sup>3</sup> have been observed.

Average (ie. *mean*) and 90th percentile concentrations (or range of concentrations) of arsenic in outdoor and indoor air in Windsor are summarized in Table 1. Estimated adult intakes per day in units of ng/day, associated with these concentrations, are also included in Table 1.

### HEALTH CONCERNS

Humans are chronically exposed to low levels of inorganic and organic arsenic in the environment. Available evidence shows that organic arsenicals in the environment, such as those found in fish and other foods, are absorbed after ingestion but have very low toxicity to humans and are excreted unchanged. These organic compounds are, on the whole, poorly characterized. On the other hand, there is considerable evidence, both from humans and from other mammals, on the toxic effects of inorganic arsenic, which is present either as trivalent or pentavalent compounds. The former are more toxic than the latter. There is, however, little information identifying exactly the inorganic compounds humans are exposed to environmentally. This is especially true of inorganic arsenic in food.

Ingestion is the main route of exposure for total arsenic in humans. The total amount ingested ranges from about 5 ug/d by a 6-month old infant to about 45 ug/d by an adult male. Food is the main source: 90% in the infant and 99% in the adult male. Intake from drinking water and soil and dust make up the balance. Inhalation is <0.1% of the amount ingested or 15 to 50 ng/d in urban environments.

Inorganic arsenic makes up about 30 to 75% of the total arsenic in food. About 90% of the inorganic arsenic in food is absorbed through the gastro-intestinal tract. The amount of inorganic arsenic ingested and absorbed is about 50% of the total arsenic, or 1 ug/d by the 6-month old infant and 15 by the adult male.



Table 1. Levels of Arsenic in Outdoor and Indoor Air in Windsor and, Estimated Intakes per day (in ng/day) Associated with these Environments.

ENVIRONMENTS	Concentration Mean or Range of Means  ng/m <sup>3</sup>	Concentration 90th percentile (or Range of)  ng/m <sup>3</sup>	Estimated Adult Range of Intakes per day  ng/day
Outdoor Air Quality - Windsor (ie. 100 % outdoor exposure) (a)	1.36 - 1.47	2.25 - 2.39	27.2 - 47.8 (a),(d)
Typical outdoor exposure (ie. = 3hr) (b)	1.36 - 1.47	2.25 - 2.39	3.4 - 6.0 (b)
INDOOR AIR ENVIRONMENTS (c) (EXTENDED periods of exposure expected) (e.g. Home, office)	0.7 - 0.9	1.6 - 2.0	12.3 - 35 (c)
INDOOR AIR ENVIRONMENTS (c) (BRIEF periods of exposure expected) (e.g. Commuting, bingo halls, taverns)	0.5	0.6 (g)	Not included (f)
<p>a) Based on 55, 24 hour average samples. Range of intakes is associated with the range of the lowest 'mean' to the highest '90th percentile' concentrations in outdoor air. It is to be noted that people are not exposed 24 hours to outdoor air. This estimation assumes 100 % exposure to outdoor air and is a measure of outdoor air quality per se and not of actual exposure.</p> <p>b) Range of intakes calculated from the lowest 'mean' to the highest '90th percentile' concentrations in outdoor air and assuming a 'typical' outdoor air exposure of = 3 hr (ie. corresponding to breathing 2.5 m<sup>3</sup>/3hr for adults).</p> <p>c) From the Windsor personal exposure &amp; microenvironment studies.</p> <p>d) Assuming an inhalation rate of 20 m<sup>3</sup>/day</p> <p>e) Range of intakes is estimated from the range of the lowest 'mean' and the highest '90th percentile' concentrations obtained from personal exposure and microenvironment measurements in indoor environments where extended periods of exposure are expected. A total exposure of 21 hours (ie. 17.5 m<sup>3</sup>/day) was assumed for these indoor environments.</p> <p>f) Direct estimation of daily intake is not appropriate since relatively small amounts of time is spent in these microenvironments.</p> <p>g) This is a maximum value.</p>			

Chronic ingestion and inhalation of inorganic arsenic at levels higher than the majority of the population of Ontario is exposed to can lead to the following effects:

- neurological, such as neuro-muscular disturbances and altered nerve conduction velocities;
- peripheral vascular changes;
- teratogenic effects (observed in animals only);
- hepatic effects, such as cirrhosis and portal hypertension.

There is sufficient epidemiological and other medical evidence that high concentrations of inorganic arsenic in water, in pesticides or in medicines cause skin cancer when ingested and that particulate inorganic arsenic causes lung cancer when inhaled. Recent studies in Taiwan for populations drinking water, with high arsenic-content, have also found significantly higher mortalities for cancer of the bladder, kidney, liver and lung. The skin cancer and the lung cancer inhalation studies are sufficient for establishing a cause-effect relationship and for deriving a quantitative dose-response function. The studies

linking internal and skin cancers to ingested arsenic have considerable uncertainties. Inorganic arsenic has been classified as a type I carcinogen (carcinogenic to humans) by IARC and as type A (human carcinogen) by US-EPA.

The epidemiological evidence for lung cancer is based chiefly on studies of workers in non-ferrous smelters in the United States, Sweden and Japan. The causal mechanisms for all forms of cancers linked to arsenic are not known, but it appears that lung cancer can be induced experimentally in small rodents.

There are no human studies on the effects of arsenic in food. However, it is known that food contains inorganic arsenic which is absorbed and presumably has the same effects as inorganic arsenic dissolved in water.

Various health criteria for inhaled inorganic arsenic (ie. Unit risks, Reference concentrations, ambient air quality guidelines) from lead agencies are summarized in Table 2. The table also includes the calculated "allowable" intake associated with the listed health criteria.

## RISK CHARACTERIZATION AND PERSPECTIVES

From the brief exposure analysis and the available health criteria the following observations can be made:

### Health messages:

- 1) All exposures are less than the chronic acceptable exposure level (ie. 10,000 ng/day) proposed by California (CDHS).
- 2) The most conservative exposure guidelines available are the potencies shown in Table 3. The carcinogenic risk associated with 'outdoor air quality' (ie. 100 % outdoor exposure) is between  $4.1 \times 10^{-6}$  and  $1.0 \times 10^{-5}$ . Similarly the risk associated with 'typical outdoor exposures' (ie. 3 hr) is between  $5.1 \times 10^{-7}$  and  $1.3 \times 10^{-6}$ . Similarly the range of risks associated with indoor air environments (ie. those in which extended periods of exposure are expected) is between  $1.9 \times 10^{-6}$  and  $7.5 \times 10^{-6}$ . The risks associated with 'outdoor air quality' are slightly higher than the risks associated with indoor air environments (ie. those in which extended periods of exposure are expected) which in turn is higher than 'typical outdoor exposures'. It should be noted that this risk characterization (ie. using carcinogenic based limits) is based on an assumed lifetime exposure (ie. 24 hours, every day, for 70 years) and hence is a very conservative assumption.

It should be noted that, although the daily intake from ingestion is much larger than from inhalation (15 ug/d vs.  $\approx 30$  ng/d), the lung cancer risk from ingestion is estimated to be less than 10% of the lung cancer risk via inhalation.

- 3) Exposures associated with indoor environments (ie. those in which extended periods of exposure are expected) exceed those associated with typical outdoor air exposures (ie. 3 hr).

### Regulatory compliance messages:

- 4) All exposures associated with outdoor air quality (ie. 100 % outdoor exposure), typical outdoor exposure (ie. 3 hr) and indoor air environments (ie. those in which extended periods of exposure are expected) fall in the lower 1 % range of air quality guidelines of various jurisdictions. All exposures are less than the Ontario guideline.
- 2) All exposures are less than the range of occupational levels.

Table 2. Summary of Exposure Guidelines for Arsenic from Leading Agencies

GUIDELINE APPLICATION	AGENCY	ORIGINAL VALUE	CONCENTRATION ("Original Form" converted to these -as applicable)			CALCULATED "ALLOWABLE" INTAKE (3)
			Unit Risk (1)	ReC (2) (1 x 10 <sup>-3</sup> )	ReC (2) (1 x 10 <sup>-4</sup> )	
INHALATION GUIDELINES						
Occupational	ACGIH, Ontario	10, NA ug/m <sup>3</sup>	NA	NA	NA	200, NA (2.8 x 10 <sup>-3</sup> )
Ambient Air Quality Guidelines	US states,	2.3 x 10 <sup>-4</sup> - 0.5 ug/m <sup>3</sup>	NA	NA	NA	0.0046 - 10 (6.6 x 10 <sup>-4</sup> - 1.4 x 10 <sup>-4</sup> )
Air Quality Guideline	Ontario	0.3 ug/m <sup>3</sup>	NA	NA	NA	6 (8.6 x 10 <sup>-4</sup> )
Chronic AELs/R/Cs	CDHS WHO	0.5 ug/m <sup>3</sup> NA	NA	NA	NA	10 (1.4 x 10 <sup>-4</sup> ) NA
Inhalation Cancer Potency Factor	EPA CDHS WHO	See Unit Risk column	4.3 x 10 <sup>-3</sup> 3.3 x 10 <sup>-3</sup> 3 x 10 <sup>-3</sup>	2 x 10 <sup>-3</sup> 3 x 10 <sup>-3</sup> 3.3 x 10 <sup>-3</sup>	2 x 10 <sup>-4</sup> 3 x 10 <sup>-4</sup> 3.3 x 10 <sup>-4</sup>	for 1 x 10 <sup>-4</sup> risk: 0.04-0.066 (5.7 x 10 <sup>-7</sup> - 9.4 x 10 <sup>-7</sup> ) for 1 x 10 <sup>-6</sup> risk: 0.004-0.0066 (5.7 x 10 <sup>-8</sup> - 9.4 x 10 <sup>-8</sup> )

1) For inhalation guidelines, unit risks are expressed as (ug/m<sup>3</sup>)<sup>-1</sup>

2) For inhalation guidelines, risk specific concentrations are expressed as ug/m<sup>3</sup>

3) Intake was computed by assuming, where applicable, an adult weight of 70 kg, a breathing rate of 20 m<sup>3</sup>/day. In all cases 100% bioavailability of the intake was assumed.

Table 3. Range of Inhalation Cancer Risks Associated with Estimated Intakes (ie. for adult exposures only) of Arsenic

RANGE of INHALATION INTAKES			POTENCY (a)		RANGE of RISKS
Environment	Unit ng/day	Unit mg/kg/day	Agency	Unit (mg/kg-d) <sup>a</sup>	
OUTDOOR AIR QUALITY (Windsor)	27.2 - 47.8	$3.9 \times 10^{-7}$ $6.8 \times 10^{-7}$	EPA	15 (a)	$5.9 \times 10^{-6}$ - $1.0 \times 10^{-5}$
			CDHS	11.6 (a)	$4.5 \times 10^{-6}$ - $7.9 \times 10^{-6}$
			WHO	10.5 (a)	$4.1 \times 10^{-6}$ - $7.1 \times 10^{-6}$
			OVERALL RANGE OF RISKS: $4.1 \times 10^{-6}$ - $1.0 \times 10^{-5}$		
TYPICAL OUTDOOR EXPOSURE (ie. ~ 3 hr.)	3.4 - 6.0	$4.9 \times 10^{-8}$ $8.6 \times 10^{-8}$	EPA	15 (a)	$7.4 \times 10^{-7}$ - $1.3 \times 10^{-6}$
			CDHS	11.6 (a)	$5.7 \times 10^{-7}$ - $1.0 \times 10^{-6}$
			WHO	10.5 (a)	$5.1 \times 10^{-7}$ - $9.0 \times 10^{-7}$
			OVERALL RANGE OF RISKS: $5.1 \times 10^{-7}$ - $1.3 \times 10^{-6}$		
INDOOR AIR ENVIRONMENTS (Extended periods of exposure expected)	12.3 - 35	$1.8 \times 10^{-7}$ - $5.0 \times 10^{-7}$	EPA	15 (a)	$2.7 \times 10^{-6}$ - $7.5 \times 10^{-6}$
			CDHS	11.6 (a)	$2.1 \times 10^{-6}$ - $5.8 \times 10^{-6}$
			WHO	10.5 (a)	$1.9 \times 10^{-6}$ - $5.3 \times 10^{-6}$
			OVERALL RANGE OF RISKS: $1.9 \times 10^{-6}$ - $7.5 \times 10^{-6}$		
a. These are equivalent potency factors calculated from the unit risks proposed by the agencies listed; assumed adult weight of 70 kg and 20 m <sup>3</sup> per day.					

3) MOEE is presently reviewing the basis of the existing standard for arsenic.

#### Summary and recommendations:

♦ All exposures are less than the chronic acceptable exposure level. Therefore, the possibility of long-term health effects, other than cancer risk, is unlikely.

♦ Since the levels of inhalation risk are less than  $1 \times 10^{-5}$ , a level generally deemed to be negligible, it is not necessary to place a high priority on exposure reduction for arsenic.

#### REFERENCES

The material in this appendix on the health concerns is taken from the unpublished report by the Standards Development Branch, MOEE - *Assessment of the toxicology, human exposure and health risks of inorganic arsenic*.





## APPENDIX 23

### RISK ANALYSIS FOR POLYCHLORINATED BIPHENYLS



## POLYCHLORINATED BIPHENYLS

### NATURE of the CHEMICAL, SOURCES, LEVELS in OUTDOOR and INDOOR AIR, and ESTIMATED INTAKES.

Polychlorinated biphenyls (ie. PCBs) are a family of chemicals that contain 209 individual compounds or congeners. These congeners are present as non-volatile, nonflammable oils or viscous liquids at room temperature or pressure. The manufacture of PCBs was banned in North America in 1977. Before the production was halted, PCBs were used as coolants or lubricators in capacitors, transformers and other electrical equipment. There are no natural sources of PCBs. Its major routes of entry into the atmosphere include leaks or fugitive emissions from PCB-containing transformers that are still in use; emissions from improperly maintained toxic waste sites or landfills that contain PCB-containing equipment; and finally environmental cycling of PCBs previously released into the environment. Environmental cycling involves the evaporation of PCBs from water and soil surfaces to the atmosphere; then the PCBs are removed from the atmosphere by rainfall or settling of dust particles; and then the cycle begins again with re-evaporation.

Average (ie. 'mean') and 90th percentile concentrations (or range of concentrations) of PCBs in outdoor and indoor air are summarized in Table 1. Estimated adult intakes per day in units of ug/day, associated with these concentrations, are also included in Table 1.

**Table 1. Levels of PCBs in Outdoor and Indoor Air in Windsor and, Estimated Intakes per day (in ug/day) Associated with these Environments.**

ENVIRONMENTS	Concentration Mean or Range of Means  ug/m <sup>3</sup>	Concentration 90th percentile (or Range of)  ug/m <sup>3</sup>	Estimated Adult Range of Intakes per day  ug/day
Outdoor Air Quality - Windsor (ie. 100 % outdoor exposure) (a)	$3.4 \times 10^{-4} - 4.3 \times 10^{-4}$	$7.7 \times 10^{-4} - 1.07 \times 10^{-3}$	$6.8 \times 10^{-3} - 2.1 \times 10^{-2}$ (a),(d)
Typical outdoor exposure (ie. ~ 3hr) (b)	$3.4 \times 10^{-4} - 4.3 \times 10^{-4}$	$7.7 \times 10^{-4} - 1.07 \times 10^{-3}$	$8.5 \times 10^{-4} - 2.6 \times 10^{-3}$ (b)
INDOOR AIR ENVIRONMENTS (c) (EXTENDED periods of exposure expected) (e.g. Home, office)	Not measured	NA	NA
INDOOR AIR ENVIRONMENTS (c) (BRIEF periods of exposure expected) (e.g. Commuting, bingo halls, taverns)	Not measured	NA	NA

a) Based on 134, 24 hour average samples. Range of intakes is associated with the range of the lowest 'mean' to the highest '90th percentile' concentrations in outdoor air. It is to be noted that people are not exposed 24 hours to outdoor air. This estimation assumes 100 % exposure to outdoor air and is a measure of outdoor air quality per se and not of actual exposure.

b) Range of intakes calculated from the lowest 'mean' to the highest '90th percentile' concentrations in outdoor air and assuming a 'typical' outdoor air exposure of ~ 3 hr (ie. corresponding to breathing 2.5 m<sup>3</sup>/3hr for adults).

c) PCBs data was not available from the Windsor personal exposure & microenvironment study.

d) Assuming an inhalation rate of 20 m<sup>3</sup>/day

## HEALTH CONCERNS

Both short-term and long-term exposures to levels at or above  $7 \mu\text{g}/\text{m}^3$  have been associated with toxic effects in both animals and humans. These effects include irritation of the eyes and skin, skin rashes, chloracne, and liver damage. However, these levels of PCBs which cause adverse health effects are much higher than the concentrations measured in the environment.

The cancer causing potential of PCBs has been examined in several epidemiological and animal studies. It has been shown to cause liver tumors in rats via the oral route of exposure. U.S.EPA ranks the family of PCBs as a probable human carcinogen.

Various health criteria (ie. Unit risks, Reference concentrations, ambient air quality guidelines) from lead agencies are summarized in Table 2. The table also includes the calculated "allowable" intake associated with the listed health criteria.

## RISK CHARACTERIZATION AND PERSPECTIVES

From the brief exposure analysis and the available health criteria the following observations can be made:

### Health messages:

- 1) All exposures are less than the chronic acceptable exposure level (ie.  $24 \mu\text{g}/\text{day}$ ) proposed by California (CDHS).
- 2) The most conservative exposure guidelines available are the potencies shown in Table 3. The carcinogenic risk associated with 'outdoor air quality' (ie. 100 % outdoor exposure) is between  $4.8 \times 10^{-7}$  and  $1.5 \times 10^{-6}$ . Similarly the risk associated with 'typical outdoor exposures' (ie. 3 hr) is between  $5.9 \times 10^{-8}$  and  $1.8 \times 10^{-7}$ . The risks associated with 'outdoor air quality' are slightly higher than the risks associated with 'typical outdoor exposures'. It should be noted that this risk characterization (ie. using carcinogenic based limits) is based on an assumed lifetime exposure (ie. 24 hours, every day, for 70 years) and hence is a very conservative assumption.

### Regulatory compliance messages:

- 3) All exposures associated with outdoor air quality (ie. 100 % outdoor exposure) and typical outdoor exposure (ie. 3 hr) fall in the lower 10 % range of air quality guidelines of various jurisdictions. All exposures are less than the Ontario guideline.
- 4) All exposures are less than the range of occupational levels.

Table 2. Summary of Exposure Guidelines for PCBs from Leading Agencies

GUIDELINE APPLICATION	AGENCY(IES)	ORIGINAL VALUE	CONCENTRATION ("Original Form" converted to these -as applicable)			CALCULATED "ALLOWABLE" INTAKE (3)
			Unit Risk (1)	R5C (2) (1 x 10 <sup>-5</sup> )	R5C (2) (1 x 10 <sup>-4</sup> )	
INHALATION GUIDELINES						
Occupational	Ontario	50 ug/m <sup>3</sup>	NA	NA	NA	1000 (0.014)
Ambient Air Quality Guidelines	US states	4.5 x 10 <sup>-4</sup> - 1 x 10 <sup>-2</sup> ug/m <sup>3</sup>	NA	NA	NA	0.009 - 0.2 (1.3 x 10 <sup>-7</sup> - 2.9 x 10 <sup>-4</sup> )
Air Quality Guideline	Ontario	0.15 ug/m <sup>3</sup>	NA	NA	NA	<sup>3</sup> (4.3 x 10 <sup>-4</sup> )
Chronic AELs/RfCs	CDHS WHO	1.2 ug/m <sup>3</sup> NA	NA	NA	NA	<sup>24</sup> (3.4 x 10 <sup>-4</sup> )
Inhalation Cancer Potency Factor	EPA CDHS WHO	See Unit Risk column	NA 1.4 x 10 <sup>-3</sup> NA	NA 0.007 NA	NA 0.0007 NA	for 1 x 10 <sup>-4</sup> risk: 0.14 (2 x 10 <sup>-7</sup> ) for 1 x 10 <sup>-4</sup> risk: 0.014 (2 x 10 <sup>-7</sup> )

<sup>1</sup>For inhalation guidelines, unit risks are expressed as (ug/m<sup>3</sup>)<sup>-1</sup>

<sup>2</sup>For inhalation guidelines, risk specific concentrations are expressed as ug/m<sup>3</sup>

<sup>3</sup>Intake was computed by assuming, where applicable, an adult weight of 70 kg, a breathing rate of 20 m<sup>3</sup>/day. In all cases 100% bioavailability of the intake was assumed.



Table 3. Range of Inhalation Cancer Risks Associated with Estimated Intakes (ie. for adult exposures only) of PCBs

RANGE of INHALATION INTAKES			POTENCY (a)		RANGE of RISKS
Environment	Unit ug/day	Unit mg/kg/day	Agency	Unit (mg/kg-d) <sup>1</sup>	
OUTDOOR AIR QUALITY (Windsor)	$6.8 \times 10^{-3}$ - $2.1 \times 10^{-2}$	$9.7 \times 10^{-4}$ $3 \times 10^{-7}$	EPA	NA	-
			CDHS	4.9 (a)	$4.8 \times 10^{-7}$ - $1.5 \times 10^{-4}$
			WHO	None proposed	-
			OVERALL RANGE OF RISKS: $4.8 \times 10^{-7}$ - $1.5 \times 10^{-4}$		
TYPICAL OUTDOOR EXPOSURE (ie.= 3 hr.)	$8.5 \times 10^{-4}$ - $2.6 \times 10^{-3}$	$1.2 \times 10^{-4}$ $3.7 \times 10^{-4}$	EPA	NA	-
			CDHS	4.9 (a)	$5.9 \times 10^{-4}$ - $1.8 \times 10^{-7}$
			WHO	None proposed	-
			OVERALL RANGE OF RISKS: $5.9 \times 10^{-4}$ - $1.8 \times 10^{-7}$		
INDOOR AIR ENVIRONMENTS (Extended periods of exposure expected)	NA	NA	EPA	NA	NA
			CDHS	4.9 (a)	Same as above
			WHO	None proposed	
			OVERALL RANGE OF RISKS: NA		
a. These are equivalent potency factors calculated from the unit risks proposed by the agencies listed; assumed adult weight of 70 kg and 20 m <sup>3</sup> per day.					

#### Summary and recommendations:

- ♦ All exposures are less than the chronic acceptable exposure level. Therefore, the possibility of long-term health effects, other than cancer risk, is unlikely.
- ♦ Since the levels of inhalation risk are less than  $1 \times 10^{-5}$ , a level generally deemed to be negligible, it is not necessary to place a high priority on exposure reduction for PCBs.

#### REFERENCES

1. Agency for Toxic Substances and Disease Registry, U.S. Public Health Service. Toxicological Profile for Selected PCBs (Aroclor -1260, -1254, -1248, -1242, -1232, -1221, and -1016). June 1989.

**APPENDIX 24**

**RISK ANALYSIS FOR MANGANESE**



## MANGANESE

### NATURE of the CHEMICAL, SOURCES, LEVELS in OUTDOOR and INDOOR AIR, and ESTIMATED INTAKES.

Manganese is a metal. In its elemental state it is a white-grey, brittle, and reactive metal that exists in many oxidation states, the most important being +2, +3, and +7.

Mn (II) are generally weakly coloured and are in many ways similar to magnesium and can replace it in some biological molecules. Mn (II) can form salts, dihalides, hydroxides and some sulphur and cyano compounds. The manganese salts are mostly water soluble with the exception of the carbonate and phosphate. Manganese dioxide found naturally is most important manganese (II) compound. It is insoluble in water and in cold acids.

Mn (III) and Mn (IV) compounds are important in photosynthesis. Mn (III) easily hydrolyses in weak acid solutions into Mn (II). Mn (IV) exists in the deep green manganate ion,  $\text{MnO}_4^{2-}$  which is stable in basic solutions only otherwise it breaks down into permanganate ( $\text{MnO}_4^-$ ) and manganese dioxide ( $\text{MnO}_2$ ). Permanganate is a good oxidant in basic solutions and is reduced to  $\text{Mn}^{2+}$  in acid solutions.

Manganese is an abundant element that constitutes approximately 0.1% of the earth's crust. A rough estimate of the average concentration of manganese in the earth's crust is approximately 1000 mg/kg. Manganese does not occur naturally in its elemental form but rather most abundantly in oxides, sulfides, carbonates and silicate compounds. It also occurs in many iron ores and other minerals. Manganese is used in the production of steel, non-ferrous alloys, dry-cell batteries, fertilizers, animal feeds, pharmaceutical products, dyes, paint dryers, catalysts, wood preservatives and glass and ceramics.

Release of manganese to the atmosphere are both natural and anthropogenic in nature. Atmospheric release of manganese, most frequently in the form the manganese oxides, is primarily through metallurgical processing, mining, steel casting and metal welding. Emissions from blast and electric furnaces can also be considerable depending on the process. Other releases of manganese to the environment included fugitive emissions resulting from material handling.

There are a number of organic forms of manganese the most relevant (important) being the cyclopentadienyl manganese tricarbonyl ( $\text{CH}_3\text{C}_5\text{H}_4\text{Mn}(\text{CO})_3$ ) also known as methylcyclopentadienyl manganese tricarbonyl (MMT). In Canada, another significant source of manganese to the atmospheric environment is MMT, the fuel additive used to reduce engine knocking. Almost all (>99%) of the MMT is combusted in the automobile engine and the principal combustion product is  $\text{Mn}_3\text{O}_4$ . The MMT that is emitted (<1%) is photochemically decomposed. Given the fact that atmospheric exposure to manganese is not likely to be to the organic form, MMT will not be considered as contributing, as part of the total exposure to manganese.

Atmospheric manganese concentrations in urban areas of Ontario range from 0.009 - 0.156  $\mu\text{g}/\text{m}^3$ . The provincial mean is 0.042  $\mu\text{g}/\text{m}^3$  (Air Quality in Ontario, 1991). The higher levels are in heavily industrialized areas and very large cities.

In the Windsor area, the average (ie. 'mean') and 90th percentile concentrations (or range of concentrations) of manganese in outdoor and indoor air are summarized in Table 1. Estimated daily adult intakes via inhalation expressed in units of  $\mu\text{g}/\text{day}$ , associated with these concentrations, are also included in Table 1.

**Table 1. Levels of Manganese in Outdoor and Indoor Air in Windsor and, Estimated Intakes per day (in ug/day) Associated with these Environments.**

ENVIRONMENTS	Concentration Mean or Range of Means  ug/m <sup>3</sup>	Concentration 90th percentile (or Range of)  ug/m <sup>3</sup>	Estimated Adult Range of Intakes per day  ug/day
Outdoor Air Quality - Windsor (ie. 100 % outdoor exposure) (a)	0.072	0.13	1.4 - 2.6 (a),(d)
Typical outdoor exposure (ie. ≈ 3hr) (b)	0.072	0.13	0.18 - 0.33 (b)
INDOOR AIR ENVIRONMENTS (c) (EXTENDED periods of exposure expected) (e.g. Home, office)	0.006 - 0.007	0.011 - 0.017	0.1 - 0.3 (e)
INDOOR AIR ENVIRONMENTS (c) (BRIEF periods of exposure expected) (e.g. Commuting, bingo halls, taverns)	0.007	0.011(g)	Not included (f)

a) Based on 2841, 24 hour average samples. Range of intakes is associated with the range of the 'mean' to '90th percentile' concentrations in outdoor air. It is to be noted that people are not exposed 24 hours to outdoor air. This estimation assumes 100 % exposure to outdoor air and is a measure of outdoor air quality per se and not of actual exposure.

b) Range of intakes calculated from the 'mean' to '90th percentile' concentrations in outdoor air and assuming a 'typical' outdoor air exposure of ≈ 3 hr(ie. corresponding to breathing 2.5 m<sup>3</sup>/3hr for adults).

c) From the Windsor personal exposure & microenvironment studies

d) Assuming an inhalation rate of 20 m<sup>3</sup>/day

e) Range of intakes is estimated from the range of the lowest 'mean' and the highest '90th percentile' concentrations obtained from personal exposure and microenvironment measurements in indoor environments in environments where extended periods of exposure are expected. A total exposure of 21 hours (ie. 17.5 m<sup>3</sup>/day) was assumed for these indoor environments.

f) Direct estimation of daily intake is not appropriate since relatively small amounts of time is spent in these microenvironments

g) This is a maximum value.

## HEALTH CONCERNS

Discussion of the adverse health effects to humans resulting from exposure to manganese will be limited to those shown to be associated with an exposure via inhalation. This discussion on health effects revolves around elemental manganese. It does not include any information that might be available on the inhalation pharmacokinetics on the major oxides of manganese.

When inhalation is the route of exposure the primary effects to humans associated with manganese are those resulting in neurological toxicity and systemic effects, specifically respiratory problems. Effects on the nervous system can, depending on degree of exposure, range from psychological disturbances that subside when removed from the manganese source, to neurological disturbances occurring due to chronic exposure. Effects associated with chronic exposure can be irreversible even when removed from the manganese source. Some common symptoms of observed early in exposure include a headache and being drowsy, followed by insomnia. With continued exposure symptoms may include speech disturbances, gait, tremor, postural instability, emotional instability, and hallucinations. These psychological and/or



neurological disturbances appear to be associated with long-term exposure to levels of manganese exceeding 250 ug/m<sup>3</sup>. Exposure to chronically high levels of manganese can lead to a severe neurological condition termed "manganism".

Reproductive effects have been shown to result when exposed to manganese. In workers exhibiting manganism, impotence and decreased libido are common effects shown. This leads to decreased reproductive success and impaired fertility. Male factory workers (age groups 16-25, 26-35) were shown to have decreased numbers of children born compared to matched control. These workers were exposed to a median concentration of 970 ug Mn/m<sup>3</sup>.

In a separate study of the same male factory workers exposed to various forms of manganese (breathing zone concentration range 70 - 8610 ug/m<sup>3</sup>, median 970 ug/m<sup>3</sup>) an increased prevalence of respiratory (coughs, acute bronchitis) and psychomotor disturbances (short-term memory, eye-hand coordination, hand steadiness) were found.

In various animal studies there is also evidence of pulmonary disturbances. In most of the animal studies these effects are evident at concentrations and exposure durations that exceed those in the human studies. There is evidence in mice that suggests that exposure to manganese *in utero* leads to neurological deficits and low birth weight in the neonate. There is significant interspecies variability but the animal data provides good supplementary information.

No studies have been identified that would suggest that manganese has genotoxic or carcinogenic potential. EPA states that it is not classifiable as to human carcinogenicity.

## RISK CHARACTERIZATION AND PERSPECTIVES

Various health criteria (ie. Reference concentrations, ambient air quality guidelines) from lead agencies are summarized in Table 2. The table also includes the calculated "allowable" intake associated with the listed health criteria.

From the brief exposure analysis and the available health criteria the following observations can be made:

### Health messages:

- 1) All exposures, except exposures associated with outdoor air quality (ie. 100 % outdoor exposure) are less than the range of chronic acceptable exposure levels (ie. 1 - 20 ug/day) proposed by California (CDHS), US EPA (IRIS) and the WHO.
- 2) Exposures associated with indoor environments (ie. those in which extended periods of exposure are expected) are similar to those associated with typical outdoor air exposures (ie. 3 hr).
- 3) All exposures associated with outdoor air quality (ie. 100 % outdoor exposure), typical outdoor exposures (ie. 3 hr) and exposures associated with indoor air environments (ie. those in which extended periods of exposure are expected) fall below the range of air quality guidelines of various jurisdictions. All exposures are less than the Ontario guideline, the basis of which is human health.

TABLE 2. Summary of Exposure Guidelines for Manganese from Leading Agencies

GUIDELINE APPLICATION	AGENCY(IES)	EXPOSURE GUIDELINE	CONCENTRATION ("Original Form" converted to these as applicable)			CALCULATED "ALLOWABLE" INTAKE (3)
			Unit Risk (1)	RsC (2) (1 x 10 <sup>-4</sup> )	RsC (2) (1 x 10 <sup>-4</sup> )	
			INHALATION GUIDELINES			
Occupational	Ontario (TWA)	100-500 µg/m <sup>3</sup> (fume + dust)	NA	NA	NA	2000 - 10000 (0.03 - 0.14)
Ambient Air Quality Guidelines	US states	0.24-500 µg/m <sup>3</sup> (annual average)	NA	NA	NA	4.8 - 10000 (6.8 x 10 <sup>-4</sup> - 0.1)
Air Quality Guideline	Ontario	2.5 µg/m <sup>3</sup> (24 hour)	NA	NA	NA	50 (7.1 x 10 <sup>-4</sup> )
Chronic AELs/RfCs	CDHS WHO EPA	0.4 µg/m <sup>3</sup> 1 µg/m <sup>3</sup> (annual average) 0.05 µg/m <sup>3</sup>	NA	NA	NA	8 (1.1 x 10 <sup>-4</sup> ) 20 (2.8 x 10 <sup>-4</sup> ) 1 (1.4 x 10 <sup>-4</sup> )
Inhalation Cancer Potency Factor	EPA CDHS WHO	NA	NA	NA	NA	NA

<sup>1</sup>For inhalation guidelines, unit risks are expressed as (µg/m<sup>3</sup>)<sup>-1</sup>

<sup>2</sup>For inhalation guidelines, risk specific concentrations are expressed as µg/m<sup>3</sup>

<sup>3</sup>Intake was computed by assuming, where applicable, an adult weight of 70 kg, a breathing rate of 20 m<sup>3</sup>/day. In all cases 100% bioavailability of the intake was assumed.

#### Regulatory compliance messages:

- 4) All exposures are less than the range of occupational levels.
- 5) Over the past decade ambient air levels of manganese have increased by 50%. This is largely due to the addition of MMT to gasoline. Higher ambient air levels of manganese are seen in industrialized cities and in large urban centres. This is likely due to both the increased number of automobiles and a larger industrial presence.
- 6) MOEE will be reviewing the basis of the existing standard for manganese.

#### Summary and recommendations:

- ♦ All exposures, except exposures associated with outdoor air quality (ie. 100 % outdoor exposure) are less than the chronic acceptable exposure level. Therefore, there is a possibility of long-term health effects, other than cancer risk, associated with outdoor air quality. It is recommended that acetaldehyde be considered a candidate for exposure reduction.

#### REFERENCES

1. Agency for Toxic Substances and Disease Registry, U.S. Public Health Service. Toxicological Profile for Manganese July, 1992.
2. World Health Organization (WHO). Air Quality Guidelines for Europe. Copenhagen, WHO Regional Publications, 1988. European Series No. 23. pp. 262 - 269.
3. World Health Organization (WHO). Environmental Health Criteria 17: Manganese. Geneva, Switzerland, 1981.
4. Ontario Ministry of the Environment and Energy (MOEE), 1992. Air Quality in Ontario, 1991.
5. United States Environmental Protection Agency (USEPA), 1990. Integrated Risk Information System: Inhalation Reference Concentration Assessment for Manganese.

